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AVIATORS "BENDS" PAIN AS INFLUENCED BY ALTITUDE AND IN-FLIGHT DENITROGENATION

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UNIVERSITY OF CALIFORNIA

MARCH 1953

WRIGHT AIR DEVELOPMENT CENTER

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AVIATORS "BENDS" PAIN AS INFLUENCED BY ALTITUDE AND IN-FLIGHT DENITROGENATION

Franklin M. Henry
University of California

March 1953

Aero Medical Laboratory
Contract No. AF 18(600)-20
RDO No. 696-61

Wright Air Development Center
Air Research and Development Command
United States Air Force
Wright-Patterson Air Force Base, Ohio

FOREWORD

Since a review of the existing literature revealed some serious gaps in the basic knowledge necessary to cope with anticipated problems, and in order to secure additional experimental facts on aeroembolism, a project identified as contract AF 18(600)-20, RDO No. 696-61, PO-12, entitled "High Altitude Physiology" was initiated. It was administered under the direction of the Aero Medical Laboratory, Wright Air Development Center, with Dr. J. W. Wilson and Major David I. Mahoney acting as project engineers.

The research work has been done by the Department of Physical Education, University of California, Berkeley, under the direction of the author. Acknowledgement should be made to the Donner Laboratory of Medical Physics for loan of the altitude chamber facility to the project, and to Dr. John H. Lawrence, M. D., and his Medical Physics staff for their helpful cooperation. Mention should also be made of Donald J. Rosenthal, M. D., who assumed the medical responsibility, Mr. Bruce M. Wilkin (a former B-24 pilot and oxygen officer) who was in charge of the operations crew during the first half of the project, and the several un-named assistants who each played an important part in securing dependable data and in maintaining an excellent safety record.

ABSTRACT

Experiments in the altitude chamber of the University of California (Berkeley) show that descent to a cabin altitude of 31,600 ft reduces the pain of aviator's "bends" to moderate severity. Below 28,000 ft the pain is mild; it disappears (on the average) at 23,900 ft. Cases of bends kept at 10,000 or 15,000 ft show a reduction in aeroembolism directly related to "storage" time; in 3 hrs there is a 13,000 ft gain in critical altitude. Frequently repeated ascent and descent does not change the critical altitude. With "storage" at 20,000 or 25,000 ft the pain altitude changes very little within 3 hrs, presumably because there is growth of sub-clinical tissue bubbles. In-flight denitrogenation for the prevention of aeroembolism symptoms should therefore be carried out at 10,000-15,000 ft. Oxygen economy can be aided by breathing cabin air at 10,000 ft during the first hour of a longer denitrogenation period on full oxygen at 15,000 ft without sacrifice of protection. Available preoxygenation tables give valid predictions if physical exertion is mild; with heavy work, considerably more denitrogenation is required. Protection is achieved by reducing symptom intensity rather than delaying onset of aeroembolism. Renitrogenation progresses as the mirror image of denitrogenation.

The security classification of the title of this report is UNCLASSIFIED.

PUBLICATION REVIEW

This report has been reviewed and is approved.

FOR THE COMMANDER:

Robert H. Blount

ROBERT H. BLOUNT
Colonel, USAF (MC)
Chief, Aero Medical Laboratory
Directorate of Research

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AVIATORS "BENDS" PAIN AS INFLUENCED BY ALTITUDE AND IN-FLIGHT DENITROGENATION

INTRODUCTION

When exposed to high cabin altitudes, some proportion of flight personnel will develop symptoms of aviator's decompression sickness (also called aeroembolism or dysbarism). At 20,000 ft the incidence of symptoms is small and incapacitation is rare; raising the altitude above this point, however, creates an increasingly grave problem. For example, at 38,000 ft, with physical activity held to a low level, about 75% of individuals will develop bends or other symptoms which will be severe enough to cause incapacitation in a third of the cases if there is no preoxygenation. With a considerable amount of physical work going on, approximately 90% of individuals will develop symptoms which will be incapacitating in half to three-fourths of the cases.

The most common symptom is aviator's "bends", typically evidenced as a deep-seated pain in or near the knee, shoulder, or other joint. Less common but more dangerous is "chokes", involving chest pain, difficulty in breathing, burning sensation in the lungs, or perhaps uncontrollable coughing. Blurred vision, blind spots or other types of impairment may occur. There may be paralysis; there may be gradual or sudden loss of consciousness, either independent of pain or as a result of severe bends pain.

Usually these symptoms disappear during descent to ground level, although the severity of chokes frequently increases during descent and visual symptoms or shock may first appear after descent is completed. The consequences of aviator's aeroembolism have seldom caused permanent injury or death, but that is because the symptoms are usually observed in an altitude chamber, where affected personnel can be quickly restored to ground level pressures. Nevertheless, serious consequences and occasional deaths from aeroembolism (dysbarism) are not unknown in the USAF (1).

The incidence of these various symptoms can be greatly reduced by several methods. Unfortunately, these methods are all subject to practical objections. Under normal modern flight conditions, symptoms are avoided by maintaining cabin pressure at a level sufficiently high to avoid aeroembolism. However, there are specific flight situations of military interest when cabin pressure may be intentionally reduced or accidently lost. To cope with these situations, it is necessary to consider and evaluate the available methods of prophylaxis.

One of these methods, preselection, will be only mentioned in passing, but it should be kept in mind as definitely of potential value (3, p. 322; 8, p. 143) if the need becomes urgent, even though it is wasteful of personnel. It may be noted that this method comes into use more or less naturally and inevitably in the routine operation of an altitude chamber.

Another method, variously called preoxygenation, denitrogenation or oxygen pre-breathing, has been considered in a recent technical report (5), with particular reference to certain flight patterns of current interest. In practical circumstances its use must be coordinated with the over-all engineering of the aircraft, since in-flight denitrogenation requires the breathing of pure oxygen and therefore the provision of an additional supply. It is not the purpose of the present study to examine that problem directly. It is intended, however, that needed background information will be developed in order to provide a basis for calculating oxygen needs in projected long range bomber flights. In particular, the report cited above presented certain tables that were probably as accurate as could be formulated from the available information. However, they involved considerable extrapolation and are therefore in need of experimental validation at points of current interest. Moreover, the amount of oxygen necessary for some particular amount of in-flight denitrogenation is dependent upon the altitude at which it occurs. While the higher altitudes are most economical with respect to oxygen supply, the decreased pressure is increasingly apt to produce rather than prevent the symptoms that are of concern. Available data have not afforded an adequate basis for deciding the optimum altitude for in-flight denitrogenation.

A third method, recompression, has received very little experimental investigation of a quantitative nature. It is important to know the minimum amount of descent that is necessary to secure partial or complete relief from aeroembolism that has developed in flight. In addition, it is of interest to discover if symptoms that are temporarily relieved by partial recompression are still potential and ready to recur immediately on re-ascent to a higher altitude, or if they become cured (either slowly or rapidly) during partial recompression. There is also need to determine just how much worse existing symptoms will become when the altitude is increased by some specified increment, and to define the range of individual differences in this relationship.

In addition to the problems outlined above, several others should be mentioned. One that is closely related to the others has to do with the so-called "silent bubbles". According to theory, the symptoms of aeroembolism are due to the growth and expansion of bubbles formed from nitrogen and carbon dioxide released from the body tissues. It is possible that exposure for a considerable time to an altitude that does not produce clinically noticeable symptoms may nevertheless initiate subclinical bubble formation, so that ascent to a higher altitude will immediately produce typical symptoms.

Another problem of concern stems from a few casual observations during the intensive aeroembolism research of the period 1942-45. With a subject in the airlock and in process of removal from the altitude chamber because of incapacitating bends, an attempt was made to determine the critical pain altitude during descent. Having made one determination, the altitude was increased until the pain returned to a moderately severe intensity and a second descent was made. This procedure was repeated several times. It was observed that the critical altitude became lower with each successive test, suggesting that rapidly repeated changes in altitude might be greatly increasing the severity of the dysbarism attack. A few scattered observations on other individuals appeared to offer some confirmation of the effect.

Quantitative information on and improved understanding of the various problems listed above should be useful in several ways. The matter of planning oxygen supplies and flight profiles for combat aircraft has already been mentioned. In addition, it should be pointed out that information of this sort should prove important in estimating the need for and effective design of certain types of emergency facilities, as for example pressurized suits or capsules. With these problems in mind, several series of experiments have been carried out and will be discussed in the following pages.

SECTION I

CRITICAL PAIN ALTITUDE

Method

"Bends" pain, the most common symptom of aeroembolism, was rated in severity by the experimental subjects themselves using a large intensity scale posted inside the altitude chamber. (A reproduction of this scale is shown in Fig. 1). The pain rating technique as developed in this laboratory was validated and extensively used in decompression sickness research during the period 1942-45 (6). It should be noted that although the descriptive terms do not seem very sophisticated, they are the ones selected from a larger number of such phrases or terms, 18 in all, on the basis of being most consistently ranked by an experimental group of 20 subjects. The need for and advantages of a multi-point objective pain scale yielding reproducible results in bends research has been expounded elsewhere (3, pp. 332-334; 8, pp. 155-159). Other symptoms such as vasomotor reactions, chokes, and disturbed vision were diagnosed and evaluated by the project physician, who observed the subjects continuously during each experiment.

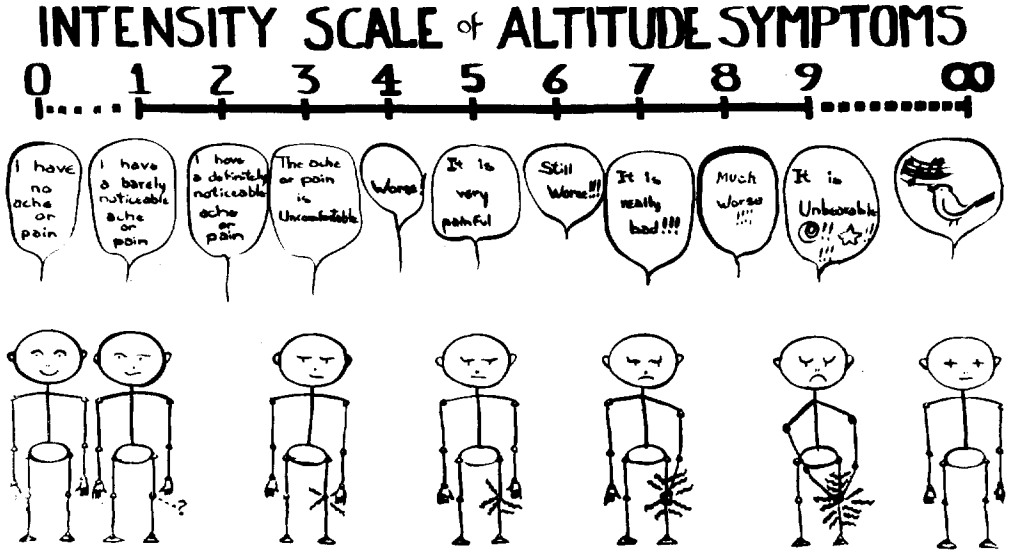

Figure 1. Pain rating scale.

All subjects were healthy young male university students, 88% in the age range 21-25 years and 98% less than age 30. They were paid $2.50 per hr for actual "flight" time. Prior to testing, each man was given a medical examination by the project physician and an indoctrination flight to learn how to use the oxygen mask and to obtain practice in clearing the ears. At that time the general nature of the experiment was explained briefly. BLB constant flow masks having light weight 2 liter rebreather bags were used, with adequate pressure to prevent inboard leakage. The oxygen was moistened to reduce discomfort.

In the "storage" and "cycles" experiments which will be described presently, the subject was taken rapidly to 38,000 ft equivalent altitude in a decompression chamber, where he performed 10 step-up exercises on a nine inch stool in 30 sec, at intervals of 2.5 min (California "D" test, 6). Upon the appearance of typical bends pain of 4° intensity (which required an average time of 18.2 min, $\sigma = 9.1$), the altitude chamber was lowered at the rate of approximately 4,000 ft/min, with the subject reporting by hand signal as the pain progressively lessened through the stages of 3°, 2°, 1°, and eventually zero. Both the inside observer and the physician observing from the outside were equipped with an altimeter placed within the field of vision, and noted the altitude (to the nearest 250 ft) at each intensity report. This test was designated "original descent".

The subject was not permitted to see the altimeter during the test; he knew only that the experiment would be concerned with varying altitudes less than 40,000 ft. Having been cleared of pain, the subject immediately re-ascended to whatever altitude produced 4° pain and descended again, with the altimeter reading recorded as before during both ascent and descent. The moment of reaching peak altitude during this test was designated zero reference time. In the "cycles" experiment, additional re-ascents and descents were performed immediately, so that 10 to 12 such tests were made during the course of an hour. In the "storage" experiments, there was an interval of some 20 to 25 min spent at a standard low altitude between successive tests, with the peak altitudes separated by 30 min.

Accuracy

The absolute accuracy of the various altitudes was controlled by using the average corrected readings of four new altimeters as a standard. Later on, a Haas standard barometer was available for checking this figure. Considering also the variability of the maintained chamber altitude, the average absolute accuracy is probably dependable within ± 85 ft at 10 to 20 thousand ft, and within ± 70 ft at 30 to 40 thousand ft. It should be mentioned that since aeroembolism is the result of a pressure differential, it was the practice to expose the men to a standard differential regardless of the ambient barometric pressure. However, the average results can be considered as absolute if the altitude of the Donner Laboratory (350 ft) is added to the reported altitudes.

Critical altitude for pre-established bends pain is considered to be the average of the altitudes at which pain of specified intensity appears during ascent and disappears during descent. Several errors are involved. There is evidence that it requires a mean time of one or two minutes for the re-appearance of a symptom on re-ascent (9; 10), and we have observed that disappearance on descent is also sluggish. (A longer time at the test altitude would of course bring in the factor of bubble growth, creating an additional error). While the cause of the pain is presumably the immediate re-expansion of extra-vascular tissue gas bubbles (3, pp. 33 and 198) since it recurs in the original site, some time is required for this pain to develop and be perceived, and there is also some lag in rating and reporting. By averaging the ascent and descent data, these errors tend to cancel out. Other sources of error include inaccuracies in quickly reading the moving altimeter pointer, and friction-induced irregularities in the pointer movement. In addition, the experimental subject's own reaction to the pain must be expected to vary from one successive test to another, and it is probable that there are also variations of a physiological nature.

The over-all magnitude of these variable errors has been evaluated by determining the test-retest correlation of individual critical altitudes, which turns out to be $r = 0.848$ for 1° pain and $r = 0.855$ for 3° pain. In the case of 1° pain the standard deviation of individual altitudes is $\sigma = 45$ mm Hg in pressure units. Computing the standard error of individual measurements as $\sigma\sqrt{1-r} = 17.5$ mm Hg, and using the curve of Fig. 2 to convert to other units, it turns out that the error is equivalent to 0.42° pain units or 1.35 thousand ft of altitude. For 3° pain, $\sigma = 43$ mm Hg, hence the standard error of measurement is 16.4 mm (equivalent to 0.82° of pain or 1.5 thousand ft of altitude).

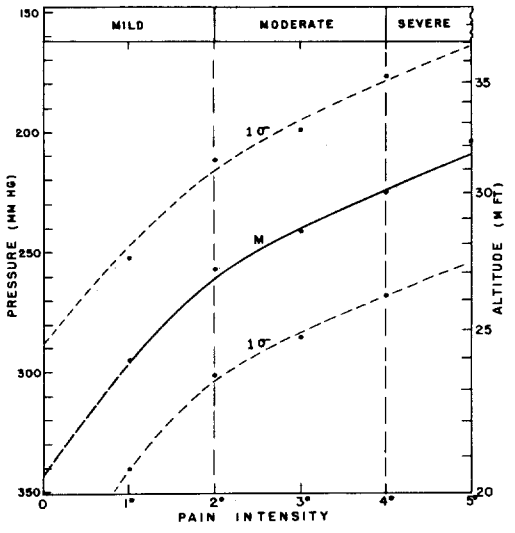

Figure 2. Mean critical altitude and fiducal limits for various degrees of pain intensity.

Psychological Controls

On seven occasions, two men who did the storage experiments simultaneously happened to have almost identical critical altitudes. At the suggestion of the project physician, several successive tests were conducted with these men sitting back-to-back. Care was taken to insure that they could not see each other's hand signals either directly or indirectly by shadows or by reflection from windows. The critical altitudes were just as similar when the men gave completely independent pain reports as they were when one man could see the other man's pain signals.

The California altitude chamber is equipped with two independent air inlets, one that is under the floor and silent in operation and another in the ceiling that causes air circulation and makes considerable noise when partly open. The vacuum line is exceptionally well silenced, and the pump is of relatively large capacity. These conditions made it possible to simulate descent while actually ascending or to simulate ascent while actually descending, insofar as external sensory cues were concerned. On some 15 occasions "inverted" inlet noises were used for an extra test made as a continuation of the regular test. While some of the men indicated surprise to find the pain increasing again, there was no evidence that the critical altitudes were influenced by the procedure.

On two occasions, when the project physician suspected that a subject was "faking" bends pain, a non-standard series of "cycles" tests was performed, using the inlet noises, slow ascent and descent, and showmanship on the part of the chamber operator, in an effort to completely confuse the subject as to altitude and climb. The pain reports continued to be made consistently.

On two occasions during the seven hour tests that will be described in Section V, the inside observer put on a pre-arranged "show" of the development of intense pain at the request of the project physician. Aided by appropriate comments over the intercommunication system, these demonstrations were very realistic, and did apparently result in one man out of eleven reporting a temporary 1° pseudo-pain.

In the light of the above observations, both the project physician and the writer are confident that the bends pains that constitute the basic data of this report are genuine pains, uninfluenced to any important degree by psychological factors such as suggestion or pseudo-pains. Various informal psychological checks in addition to those mentioned have been made; quite uniformly, we have found that our suspicions of invalid pain reports during the experiments have proved to be without foundation.

Experimental Results

Figure 2 gives the critical altitudes for different pain intensities for 56 men who were tested 30 min after the original descent from 38,000 ft. The reason for choosing this particular time is that the critical altitudes are then lowest, as will be explained below. Thirty-three of the men had two such tests, which were averaged to secure the individual mean scores. Since it was only intended to let the pain develop to 4° intensity, the observation of 5° pain was uncommon and only occurred in 12 cases. The average altitude increment for the 4°—5° step was computed for these 12 men and added to the 4° average for the entire group, to give an adjusted mean for 5° pain.

Critical altitudes for the other four pain intensities were determined by plotting the individual scores (ascent and descent averaged) as cumulative frequency graphs on probability coordinate paper, and fitting a smooth curve to the points. These curves were in turn used for determining the mean and standard deviation to give the plotted points of Fig. 2 and the entries in Table 1. There is reason to believe, as explained below, that the 5° symptom represents a practical critical altitude in that greater intensities than this can be expected to result in non-functional personnel.

Table 1

CRITICAL ALTITUDE OF PRE-ESTABLISHED BENDS PAIN

For various intensities of pain, in thousands of feet, as exhibited by the specified percentage of individuals in the sample (n=56)

Intensity	Cumulative per cent								
	10%	20%	30%	40%	50%	60%	70%	80%	90%
1°	19.7	21.2	22.2	23.0	23.9	24.7	25.8	26.8	28.6
2°	22.6	24.0	25.2	26.2	27.1	28.1	29.2	30.6	32.7
3°	23.9	25.3	26.5	27.5	28.5	29.5	30.7	32.1	34.3
4°	25.5	26.7	27.7	28.8	30.1	31.3	32.6	34.3	36.9
5°	26.6	27.9	29.2	30.4	31.6	32.9	34.3	36.0	38.7

A conventional clinical interpretation of the pain intensity scores is shown at the top of Fig. 2. It is the opinion of the project physician that about half of the observed 4° pains should be classed as severe, so this has been taken as one of the transition points; similarly, at least half of the 2° symptoms are considered by him to be clinically moderate pains, so this is taken as the other point of transition. It may be mentioned that in the 1942-45 research at this laboratory, using the same pain rating system, the subjects remained at high altitude until incapacitated (6). Pain within the 3°—5° range was typically found associated with impaired function, but only rarely with real incapacitation. More than half of the 6° symptoms were found to be associated with real incapacitation, so the 5°—6° region can be considered another clinical reference point.

Conclusions from the data will in general be based on analysis of 1° pain reports and also 3° pain reports (as in our other publications), with the implicit assumption that it should thereby be possible to estimate the probable situation with severe symptoms. In the present series of studies we were not permitted,

for reasons of safety, to carry the symptoms to high intensities. It is thought that the complete absence of severe post-flight reactions and hospitalized cases, in marked contrast to our 1942-45 experience, is due to this enforced experimental caution.

SECTION II

EFFECT OF REPEATED ASCENTS AND DESCENTS

"Cycles" Experiment

Immediately following the development of typical bends pain at 38,000 ft and test zero, 11 men were individually subjected to the "cycles" experiment mentioned previously. Variations in the individual critical altitudes for 1° pain as a function of time are shown in Fig. 3. Points on these curves were obtained by averaging the ascent and descent data for each cycle. Similar graphic analysis has also been done for 3° pain, with essentially the same pattern of results at an altitude about 4,500 ft higher. It may be seen that all of the subjects exhibit a lowering of the critical altitude during the early part of the period, reaching a minimum followed by a rising phase indicative of symptom decay. On the average, the minimum is reached 26 min after test zero which corresponds to 40 min after symptom onset at 38,000 ft. The average of the minimum critical altitudes is 21.4 thousand ft ($\sigma = 4.3$).

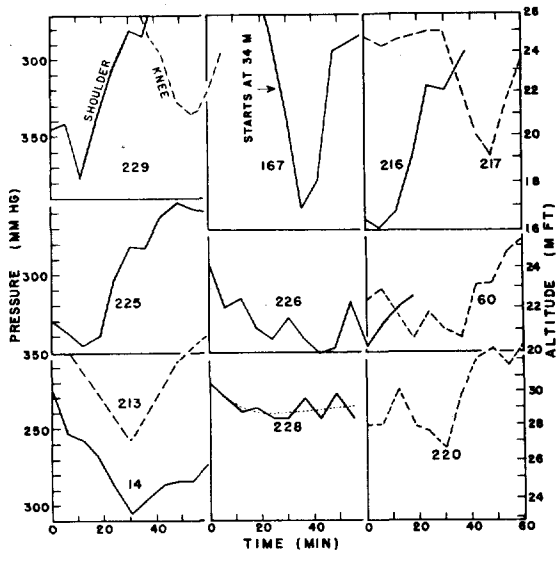

Figure 3 Individual curves of symptom growth and decay during cycles experiment.

In order to compare these data with the critical altitudes obtained in the absence of the cycling procedure, it is necessary to cross-section the "cycles" data at the time of the average minimum. At this point, the average critical altitude is 24.4 thousand ft, a figure which does not differ significantly from the average of 23.9 for 1° pain shown in Table I ("t" = 0.58). By a fortunate coincidence, these latter data were secured at a corresponding time, namely 41 min after symptom onset at 38,000 ft or 30 min after test zero.

The average altitude prevailing during the cycling procedure (i.e., the average of the highest and lowest altitudes reached during a cycle) was 28.0 thousand ft at test zero and 26.7 thousand ft at the average minimum. Since this is fairly close to the altitude at which one series of 21 subjects was "stored" for a period of 30 min following test zero, (25.7 thousand ft corrected altitude), it is perhaps more valid to compare the latter data with the cycles experiment. The average critical altitude for the test after 30 min storage was in this case 24.7 thousand ft (σ = 4.1), which is again not significantly different from the cycles result ("t" = 0.17). It may therefore be concluded that the repeated variation up and down in altitude that characterizes the cycles test is without influence on the critical pain altitude.

The data of Fig. 3 are useful in illustrating the growth and decay process of individual symptoms. Considerable variation is apparent--in subjects Nos. 216, 220, 225 and 229, for example, the major part of the growth had occurred before test zero. Some individual records, for instance Nos. 167 and 217, show a large and rapid growth and decay, whereas others, such as Nos. 60, 226, and 228 are characterized by a relatively flat curve. One case, No. 229, is of particular interest in illustrating that the curves of two different symptoms in the same individual may vary quite independently. The average decrease in critical altitude from test zero to the individual minimum points is 4.8 thousand ft, and at the average time of minimum altitude, 1.8 thousand ft. These curves are very similar to symptom growth curves obtained by an entirely different method that have recently been published in another report (5, p. 14).

SECTION III

STORAGE EXPERIMENTS

Method

In these experiments, typical bends pain was induced as in the "cycles" tests, and following test zero the subjects were "stored" at 10,000, 15,000, 20,000 or 25,000 ft for 3 hrs. At intervals of 30 min, a quick test ascent to whatever altitude produced 4° pain (or to 40,000 ft maximum), was made and followed by immediate descent. In the case of the lower storage altitudes the rate of ascent and descent was 5 to 6 thousand ft/min up to the expected region of pain appearance and 3.5 to 4 thousand ft/min thereafter.

The "ascent" and "descent" data for 1° and 3° pain were plotted separately on probability graphs as shown in Fig. 4, using pressure ordinates rather than altitude ordinates since the former result in statistically normal frequency distributions whereas use of the latter causes the distribution to be skewed.

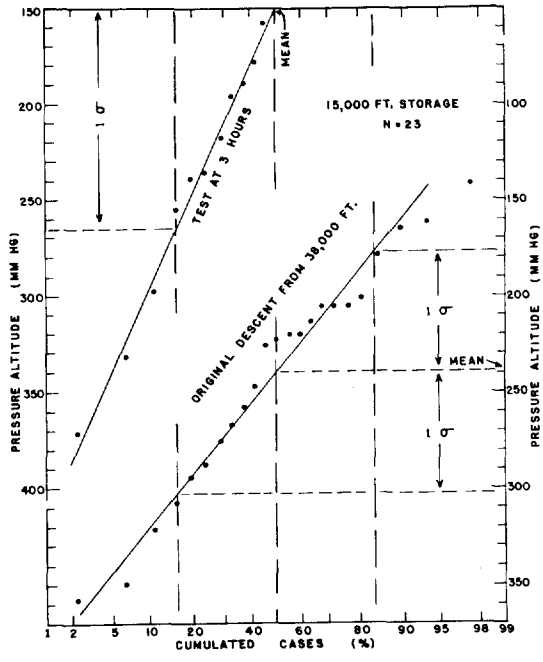

Figure 4. Individual data on change in pain from 3° to 2° intensity during descent.

In one of the examples shown, namely "original descent", it would have been possible to use the conventional numerical method for computing the mean and standard deviation since scores are available for each individual tested. In the other example, showing the results for the test made after three hours storage, it can be seen that the conventional method would give erroneous results. Half of the individuals tested at this time did not develop 3° pain at the maximum test altitude of 40,000 ft and therefore cannot be given numerical scores. It is possible, however, to plot the points that are available, and by fitting a smooth curve, the mean and standard deviation (σ) can be determined graphically as shown.

In plotting these data the mid-frequencies have been used; e.g., the first, second and third individuals in the example have been assigned cumulative frequencies of 2.2, 6.5, and 10.8% rather than 4.4, 8.7 and 13.0%. The mean is of course the 50th percentile, while the standard deviation is the intercept at the 15.9 or 84.1 percentile. Having determined the ascent and descent statistics separately, the two were averaged to give the critical altitude for 1° or 3° pain as the case might be.

From 20 to 23 men were tested at each storage altitude. In a number of cases, the same individual was tested in more than one series, the amount of overlapping of this type being 33% between the 10,000 and 15,000 ft series and 45-50% between the others. It may be seen in Fig. 5 that the groups were not perfectly matched in initial critical altitude. However, the differences may safely be disregarded. They are no greater than would be expected from random sampling, since a variance analysis of the original descent scores yields an "F" of only 2.46 for 1° pain and 2.26 for 3° pain, whereas an "F" of 2.75 would be required for statistical significance. The "F" coefficients at the 30 min test are also non-significant (1.27 and 1.21).

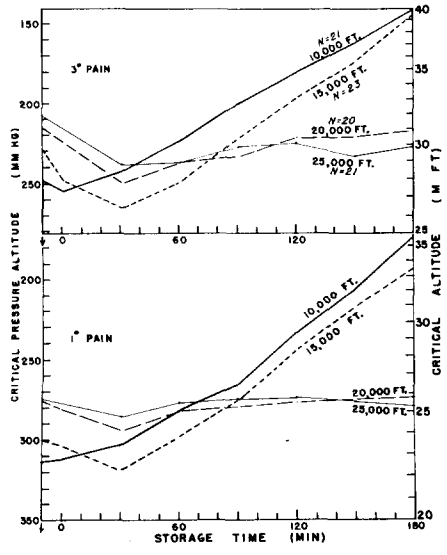

Figure 5. Symptom growth and decay at storage altitudes.

It should be mentioned that the mean critical altitudes for original descent (↓) were necessarily determined without averaging with ascent data. The points as plotted for this particular coordinate are adjusted means, obtained by using the 30 min test as a reference point and subtracting from this the pressure increments between original descent and 30 min descent.

There was no test zero for many of the men in the 20,000 and 25,000 ft series (these were chronologically the first experiments). For this reason, a clear cut statistical evaluation of symptom growth during the first 30 min of storage must be limited to a comparison of the change in "descent" critical altitudes only, using the differences between original descent and the 30 min descent.

Symptom Growth and Decay During Storage

Pooling data for the 15, 20, and 25 thousand ft storage series (since all three show similar declines), the evidence is clear that symptom growth occurs during the first 30 min of storage at these altitudes. (The "t" ratio for altitude change for 1° pain is 2.6 and for 3° pain is 5.5). In the case of the 15,000 ft storage experiment treated separately, the decline is not statistically significant for 1° pain ("t" = 1.4), but is definitely significant for 3° pain ("t" = 3.7). (For groups of the sizes used in this test, a "t" of 2.09 is required for statistical significance). There is no evidence of symptom growth in the 10,000 ft storage experiments.

Persistent or intermittent 1° and 2° pain was fairly common during storage at 25,000 ft (33%) and 3° pain was sometimes observed (24%). Three of the men had to be kept at substandard altitude during part of the storage, in order to keep the pain below 4°. (In two additional cases, not included in the statistics of Fig. 5, the pain was so severe that storage was impossible. Inclusion of these in Table 3 would not alter the percentage figures). At 20,000 ft there were three cases of 1° pain lasting for $\frac{1}{2}$ to 1 hr, but no 2° pain. In the 15,000 ft series one individual had 1° pain intermittently during the first 30 min of storage. No pain was observed during storage at 10,000 ft.

Table 2 gives the critical altitude range that includes 68% of cases, as determined by the six tests, for each of the different storage series. The two points for each test may be plotted at $\pm 1\sigma$ on a probability graph such as shown in Fig. 4 and connected by a straight line, yielding a curve that permits the construction of detailed tables of the range of individual differences comparable to Table 1.

Turning now to the evidence for symptom decay during the main part of the storage period, it may be seen in Fig. 5 that the rising trend indicative of this process is unmistakable for the two lower altitudes, and almost completely absent for the two higher altitudes.

A statistical analysis of the 25,000 ft storage series shows no significant change in critical altitude between the 30 min and 120 min tests for either 1° or 3° pain. (This comparison is between the points of greatest difference). In contrast, the 20,000 ft data for both 1° and 3° pain show a statistically significant rise in critical altitude at 60 min and every test thereafter, compared with the 30 min test as a reference point. While the rise is consistent, it is small in amount. Apparently the tendency for symptom decay after the initial growth period is almost exactly balanced by continuing growth at 25,000 ft, during the limited period of observation. Another and more attractive explanation would be that "silent" intravascular gas bubbles are interfering with denitrogenation (2). This hypothesis, however, seems untenable because direct measurements of nitrogen gas excretion show no change up to 35,000 ft and an increase at higher altitudes (3, p. 310; 8, p. 56).

Table 2

FIDUCIAL LIMITS ($\pm 1\ \sigma$) OF CRITICAL PAIN ALTITUDE

The tabled figures are in thousands of feet. Altitudes higher than 40,000 ft were obtained by extrapolation.

Storage Altitude	Storage time in minutes (3° pain or worse) 30	60	90	120	150	180
25,000	24.8 33.5	24.7 33.8	25.2 35.2	25.1 36.1	24.2 35.6	24.3 36.7
20,000	22.6 34.3	22.0 38.2	22.3 38.6	23.0 40.8	22.5 41.9	22.9 42.3
15,000	21.8 31.7	22.5 34.4	24.6 37.4	25.2 44.6	26.5 50.8	28.0 64.5
10,000	23.4 34.4	24.9 36.7	26.6 40.8	28.4 43.7	30.5 46.3	32.6 51.3
10,000 (air)	25.1 35.2	27.2 38.6	28.1 40.8	29.1 41.3	31.1 42.8	30.8 43.7

Storage Altitude	Storage time in minutes (1° pain or worse) 30	60	90	120	150	180
25,000	20.9 29.0	21.5 30.0	21.5 30.5	21.2 30.8	20.2 32.0	19.5 32.4
20,000	20.0 28.7	20.2 30.7	19.5 32.5	18.9 33.8	18.5 35.1	18.1 36.0
15,000	18.0 27.0	19.4 28.8	21.0 31.1	21.6 37.3	22.5 43.3	24.0 48.9
10,000	18.3 29.3	19.2 30.8	20.5 33.7	22.8 37.8	24.5 42.2	26.2 51.5
10,000 (air)	21.0 29.2	23.3 32.5	23.6 35.3	24.2 36.1	25.1 35.8	25.3 37.0

There is evidence from other studies (5, p. 13) using a different technique, that the growth-decay curve shows a later and more gradual peak as physical activity is decreased and experimental altitude is lessened, so the present results are not entirely unexpected. It seems very likely that with a considerably longer period of observation, the 25,000 ft data would have exhibited a symptom decay phase evidenced by a rising critical altitude. As a matter of fact, examination of individual curves reveals that 11 of the 21 individuals in this series do show definite indications of symptom decay, although the averaging procedure obscures this observation. (It will be recalled that the "cycles" experiment illustrated the wide differences in individual growth-decay curves). Evidently the region of 20-25 thousand ft is the altitude of slowest symptom decay. At higher altitudes, there is an increasing apparent acceleration of both the growth and decay factors, while at lower altitudes the growth factor begins to disappear, so that only the decay phase is operative. In this instance the decay phase can occur only when there are pre-existing tissue bubbles initiated at some higher altitude. At lower storage altitudes, the factor of re-compression would be expected to assume an increasingly important role in adding to the symptom decay resulting from the denitrogenation that occurs at all altitudes (providing that alveolar nitrogen is absent or at low tension).

At 15,000 ft storage, there is still a symptom growth phase as mentioned earlier. It is becoming less evident than at higher altitudes and is apparently non-existent in the 10,000 ft experiments. The amount of re-compression is of course greater at 10,000 ft. There is no alveolar nitrogen tension at either of these altitudes under the conditions of the experiment. It would be expected, therefore, that symptom decay would be greatest during the 10,000 ft storage procedure. However, the data exhibited in Fig. 5 fail to agree with this hypothesis. There is no statistically significant difference between the results at 10,000 ft and 15,000 ft for either 1° or 3° pain, analyzed as "gain in altitude" from original descent to the 180 min test or as gain in altitude calculated from the low point at the 30 min test ("t's" range from 0.8 to 1.1). In another analysis of these data, the individual critical altitude curves have been ranked in accord with the amount of individual symptom decay. A chi-square comparison of the results at the two altitudes shows no differentiation ($\chi^2 = 0.4$). Evidently the increased re-compression at 10,000 ft compared with 15,000 ft is not important in producing any more rapid symptom decay. This matter will receive further discussion below.

Oxygen vs. Air During Storage

In order to study this situation further, an additional 10,000 ft storage experiment was performed, with the men breathing ambient (cabin) air except at altitudes above 12,000 ft during the brief high altitude tests. Fifteen of the 21 subjects were tested in both experiments (71% overlapping), so the two series were very closely matched. (The critical altitudes at initial descent, and also at test zero, differ in the two series by only 10 mm pressure). The comparative results of storage under the two conditions are shown in Fig. 6. At the 60 min test, the critical altitude for the "air" storage appears to be somewhat higher, but this difference is within the limits of sampling error since "t" is only 1.3 for 1° pain and 0.6 for 3° pain. After 3 hrs the critical altitude is lower in the case of air breathing, and the difference is statistically significant ("t's" = 2.4 and 2.3). The rate of symptom decay is therefore maintained after the first 60 min when oxygen is breathed during storage, whereas it declines sharply after this time when breathing ambient air.

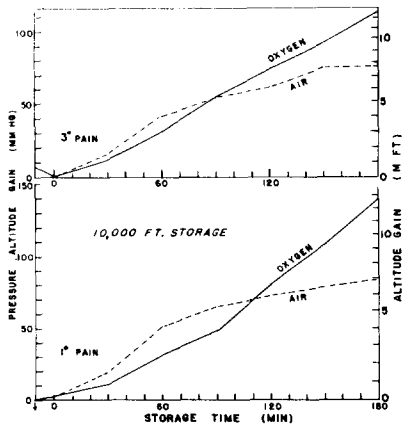

Figure 6. Air vs. Oxygen during storage.

As a further statistical check, individual curves (averaging 1° and 3° data) for both series were ranked according to rate of symptom decay for the first half and separately for the second half of the storage period, and then analyzed by the chi-square test. For the first half, the two series do not differ significantly ($\chi^2 = 0.9$). For the second half, the difference is definitely significant ($\chi^2 = 6.1$). With oxygen breathing, there is no appreciable difference in the rate of symptom decay during the first and second halves of the storage period ($\chi^2 = 1.5$). When ambient air is breathed, this difference is significant ($\chi^2 = 6.1$); the rate of decay is very slow during the second half. The only intentional experimental variable is alveolar nitrogen tension, which is approximately zero for oxygen breathing and about 400 mm when ambient air is breathed. In the latter case there is of course some hypoxia; the lips and fingernails of several of the men were definitely cyanotic.

Considering the results at 15,000 ft and 10,000 ft breathing oxygen, the evidence forces the conclusion that during the first hour the rate of symptom decay is independent of re-compression differences. At 10,000 ft, breathing pure oxygen causes no more symptom decay than breathing ambient (cabin) air during the first 1 or $1\frac{1}{2}$ hrs even though it creates a greater nitrogen differential.

These findings can be reconciled with current theory, if it be postulated that both the 15,000 and 10,000 ft altitudes result in pressures greater than the critical amount for bubble growth (3, p. 202 ff.), which is quantitatively a more important factor than the relatively small differences in resorbtion rates caused by the ambient pressure differences. The other factor to be considered is that the denitrogenation rate at 10,000 ft on air is faster than the "normal" rate. Jones (3, p. 310) as well as others (3, p. 142) have remarked on the fact that mild hypoxia produces a large increase in the denitrogenation rate. It can be seen in Fig. 6 that the trend of the data is in the direction predicted by this factor; the more rapid gain in critical altitude while breathing air during the first hour certainly suggests that this group is denitrogenating as fast or faster than the oxygen-breathing group. Evidently the greater nitrogen differential when breathing oxygen is more than counterbalanced by the greater rate of gas exchange while on air at 10,000 ft during the early stage of denitrogenation. The effect is limited, of course; at 10,000 ft not more than 36% protection could be achieved with unlimited time. Assuming that the rate is increased to 30 min half-time (which is a reasonable assumption) 90% of this possible protection

would be reached in 1½ hrs; this is just about the course of events shown in the "air" curve of Fig. 6. After this length of time, the nitrogen differential becomes increasingly important in accordance with standard theory. The experimental results suggest that in-flight denitrogenation for the purpose of bends prophylaxis might be as effective on ambient air as on oxygen during approximately the first hour of the denitrogenation period.

It would seem reasonable to contend that a somewhat higher cabin altitude might be desirable during the last half hour or so of the air-breathing denitrogenation period; both the increased hypoxia (provided it is not excessive) and the greater nitrogen differential from the lowered air pressure would improve the effectiveness. No doubt 12,000 ft could be used without running into difficulty; possibly even 14,000 ft near the end of the period if the air crew was acclimatized to some degree.

"True" Critical Altitude of Aeroembolism

To interpret the data properly, some allowance must be made for the fact that the effective storage altitude must have been greater than the base-line, because the tests made at 30 min intervals exposed the subjects briefly to much higher altitudes. By estimating the area of each individual flight profile it is possible to adjust the base-line to an average corrected altitude for each series, namely 14,200, 17,800, 21,500 and 25,400 ft. These corrections necessarily are only approximations, but they probably yield more accurate reference points than the nominal storage altitudes.

Using these figures, and averaging the 1° and 3° data for maximum gain in critical altitude resulting from symptom decay during 3 hrs, the smooth curve of Fig. 7 has been constructed to define what might be termed the critical altitude for aeroembolism. (A comparable curve using the gain between test zero and the 180 min test is very similar). It is probably a region rather than a sharply demarked point, and may vary between individuals as well as with the experimental conditions. The present study places the average critical region between 18,000 and 21,000 ft, which is in excellent agreement with other studies using entirely different methods (3, pp. 217-218). It is somewhat lower than the mean critical altitude of 23,900 ft for pre-established bends pain reported earlier in the present study, but this should occasion no surprise since there is ample reason to believe that the physiological basis of decompression sickness exists at sub-clinical levels. The storage experiments, being concerned with "silent" symptoms, prove this point very effectively. There was no clinical evidence whatever of aeroembolism at the lower storage altitudes while the men stayed at those altitudes, yet the evidence shows that the disease changed in severity with the passage of time even though clinically "silent".

Results of Other Investigators

The results secured in a study by Fraser (2) on stepwise ascent may be compared in some respects with the current data. He used 1 hr at ground without oxygen or 1 hr at 10,000, 20,000 or 27,500 ft with oxygen, followed in each case by 2 hrs at 35,000 ft. Using the non-denitrogenated ground level group as a control, the total symptom incidence was reduced to 45% of the standard in the

10,000 ft series; 65% in the 20,000 ft series, and 70% in the 27,500 ft series. Considering only moderate or severe symptoms, the figures were 27, 44, and 70% of the control incidence.

Fraser attributed the higher incidence with the 20,000 and 27,500 ft "steps" to the formation of silent bubbles that interfered with the denitrogenation process. Whether this hypothesis is accepted or not, the results do show without question that in-flight denitrogenation is less effective at 20,000 ft or higher than is the case at 10,000 ft. The relative incidence of total symptoms with the 10,000 ft step is very close to the prediction of 55% obtained from the Jones tables (3, p. 318; 8, p. 98); moderate and severe symptoms have been reduced more than the average expectancy for one hour of ground level denitrogenation. Gray (4) observed that ¼ hr of denitrogenation at 14,250 ft was as effective as at ground level, whereas at 19,250 ft or higher it was less effective. These studies agree in indicating that in-flight denitrogenation at 10,000 and probably 15,000 ft is no less effective than at ground level.

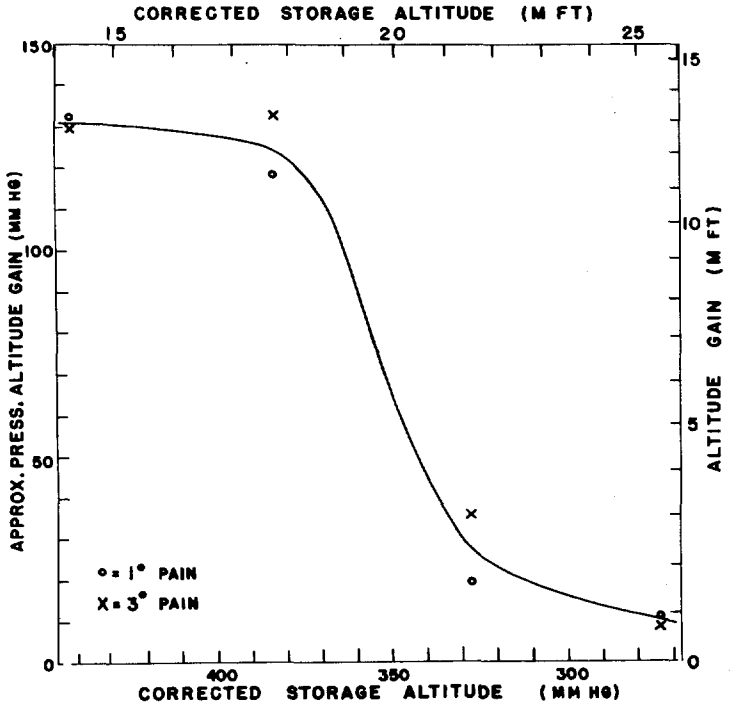

Figure 7. Symptom decay related to storage altitude.

Individual Differences

Some interesting side-lights of the storage experiments justify additional comment. One such matter has to do with the question of whether individuals who exhibit a low critical altitude during the early part of storage show more or less symptom decay than those who have a relatively high critical altitude. Using the 15,000 ft storage data, the 12 "lowest" and 12 "highest" individuals were compared for amount of symptom decay. For 1° pain, X^2 was 0.4, and for 3° pain it was 2.1. Neither of these statistics is significant. If there is any difference, it is apparently not of much importance.

There are fairly consistent individual differences in the rate of symptom decay at the lower storage altitudes. Pooling the 10,000 ft and 15,000 ft data, there are 26 cases who had storage tests on two separate occasions. For each series, individual decay curves have been ranked as above or below average for that series. It turns out that 77% of these men hold their relative positions as having a "fast" or "slow" curve in both tests. A chi-square analysis gives $\chi^2 = 6.4$, which is highly significant statistically, and corresponds to a correlation coefficient of $r = 0.74$. Presumably these differences are due to individual differences in rate of nitrogen clearance.

The reproducibility of individual critical altitudes from one day to another is somewhat less than this, namely $r = 0.73$ for 1° pain and $r = 0.73$ for 3° pain during original descent from 38,000 ft. As might be expected, this day-to-day reliability is somewhat less than is the case for two successive tests made on the same day. Earlier in the report, the reliability of the latter was found to be $r = 0.85$ for 1° pain and $r = 0.86$ for 3° pain.

Percent Recurrence After Storage

It is possible to compare certain of the data secured in the present experiments with results obtained by others, although it is necessary to limit the comparison to relatively crude descriptive statistics. Stewart and Smith in 1943 (10) reported that the recurrence of pre-established decompression sickness, tested by re-ascent after storage at ground level for ½ to 1 hr breathing air, was 100%. This is in sharp disagreement with results reported by Rodbard in 1944 (9); the latter investigator found only 50% recurrence. With 1½ to 2 hrs storage, the Stewart and Smith finding is 75% recurrence of pain in the original site compared with 52% reported by Rodbard; with 2½ to 3 hrs storage the figures are 77% and 38%. The Rodbard data show a statistically significant difference from the others in each of these comparisons. A possible explanation of the discrepancy is that the method and criteria for bends were different in the Rodbard study. Reference was made earlier to the necessity for a standard methodology in bends research. In the present investigation, 10,000 ft storage breathing ambient air (with, of course, less re-compression) resulted in 98% recurrence after ½ to 1 hr, 74% after 1½ to 2 hrs, and 67% after 2½ to 3 hrs storage.

Stewart and Smith also made a few observations on storage at several higher altitudes. Four men were stored at 25,000 ft for 30 min with complete recurrence and 16 men were stored at 20,000 ft for periods running from 30 to 120 min with complete recurrence. Without question, these findings agree with the present study (Table 3). Nine men were stored by them at 15,000 ft for 30 min, with only 44% recurrence--much lower than the amount of recurrence at the same altitude in the present experiment or in their storage at ground level or at higher altitudes. Due to the small number of individuals, which results in a large sampling error, it is doubtful if much significance should be attached to their 15,000 ft experiment. In Section VI of the present report it will be shown that the proportion of recurrence as a function of time, in the case of both 10,000 and 15,000 ft storage on oxygen as reported in Table 3, decreases in accordance with denitrogenation theory.

Table 3

PER CENT RECURRENCE OF ESTABLISHED BENDS PAIN

Storage Altitude	Storage time in minutes (3° pain or worse) 0	30	60	90	120	150	180
25,000	100	95	95	95	95	91	91
20,000	100	90	85	85	80	80	80
15,000	100	100	96	87	74	61	52
10,000	100	100	91	81	57	43	38
10,000 (air)	100	100	95	76	71	67	67

Storage Altitude	Storage time in minutes (1° pain or worse) 0	30	60	90	120	150	180
25,000	100	100	100	100	95	100	95
20,000	100	100	100	90	90	85	85
15,000	100	100	100	100	91	83	65
10,000	100	100	100	91	86	67	57
10,000 (air)	100	100	100	100	95	86	86

Comment on Reproducibility

The "California D" test, used to initiate bends pain in the current storage experiments, has in other investigations been reported to produce an incidence of 87% total symptoms, usually within the first 45 min, with 90% of the cases progressing to 3° or worse (3, p. 231; 6, pp. 42 and 48). In the unselected group used in the present experiments, 89 men had an original 38,000 ft "D" exposure of 30 min or somewhat longer to pre-establish the bends studied in the storage or cycles series. The total incidence was 89% with 84% of the cases progressing to 3° or worse. (A similar correspondence is evident between the light exercise series to be discussed in Section V and an earlier California study). The remarkably close agreement between the incidence in these two studies (separated in time by about ten years) is mentioned here in order to establish that the subjects of the present study constitute a representative group, and to emphasize that it is possible to secure reproducible results in aeroembolism research if meticulous attention is given to the standardization of methodology. Lack of such standardization has greatly limited the usefulness of experimental work (otherwise sound) done in different laboratories (e.g. 5, p. 21. Also see 3, pp. 225 and 332 ff. or 8, p. 154 ff.).

The primary datum in human aeroembolism is the pain experienced by the person himself. This is, of course, subjective, but is adequately consistent if proper psychological conditions are maintained. It is not consistent or quantifiable if they are not maintained.

If the men undergoing the experiment are oriented to hide their pain, either by direct instruction or by the general atmosphere of the procedure, some individuals will do so and some will not, hence the resulting data will include an additional (although avoidable) source of error variance as well as systematic error. If the orientation is intentionally or unintentionally in the direction of over-emphasizing the severity of symptoms or the danger involved, (as may well occur for example under poor psychological conditions or in improperly indoctrinated groups) there will be an additional avoidable source of error variance and systematic error. Data biased by these errors are very difficult to interpret; one can only guess at the quantitative influences of the biasing factors.

Beyond the primary datum, it is possible to maintain objectivity, but this can be accomplished only if the subjective influence of the experimenter is rigorously excluded. There is, unfortunately, a constant temptation for the experimenter to decide how severe the pain must have felt to the subject, but any such decision constitutes a secondary datum involving two subjective elements. These simple straightforward facts cannot be avoided by limiting the reports to severe pain. Such a procedure may even make the situation worse from the point of view of securing reproducible data. The experimenter can measure rather accurately (although not very practically) how many men lose consciousness in an aeroembolism experiment. However, he cannot know if a man who is "putting on a show" is suffering either more or less acutely than some other individual who quietly signals a pain of the same intensity, or is closer to or further from complete collapse, unless he secures evidence to validate his opinion, and keeps record of his failures as well as his successes. (Such a record is illuminating, although not very flattering).

Evidence is available to validate the above-mentioned primary data in a practical frame of reference. Motor impairment, rated during muscular activity by an experienced observer without knowledge of the degree of pain reported by the man suffering from bends, has been found to correlate r = 0.90 with the pain as evaluated by the method used in the present investigation (6, p. 37).

SECTION IV

SILENT BUBBLE EXPERIMENTS

Formation at 15,000 Feet

The experiments previously described have furnished ample evidence of the existence of "silent" extra-vascular tissue bubbles present at storage altitudes as residual from an immediately preceding higher altitude exposure (also see 3, pp. 33, 193 and 197 ff.). Some additional data have been obtained under conditions where the initial bubbles are established at the storage altitude. Since the other experiments clearly indicated bubble growth at 21,500 ft and 17,800 ft, with no growth at 14,200 ft (corrected altitudes) it was decided to use a storage altitude of 15,000 ft. Interest had also been directed to this particular altitude as the highest that could safely be used for in-flight denitrogenation purposes. There was no pre-storage exposure to higher altitude, and the "tests" were reduced in number and spaced further apart so that the nominal storage altitude would be very nearly the same as the effective altitude.

With indications that there would otherwise probably be no silent bubbles, it seemed desirable to use exercise as a facilitating agent to start bubble production. Twenty-one men exercised at $2\frac{1}{2}$ min intervals for the first $\frac{1}{2}$ or 3/4 hr of exposure (using the standard 10 step-ups mentioned in connection with other experiments) and 11 men exercised in the same manner but at 5 min intervals for $1\frac{1}{4}$ hrs.

The last-mentioned group of 11 men had no bends symptoms when tested with a quick test climb to 40,000 ft after exposure times of $1\frac{1}{2}$, 3 and 4 hrs, with the exception of one man who had a 1° knee pain that came in at 38,000 ft on the first two of these tests.

Among the men who exercised more frequently but for a shorter time, five exercised for $\frac{1}{2}$ hr and were given the high altitude test at half-hourly intervals for 4 hrs, with no symptoms. Ten exercised 3/4 hr and were given the test at hourly intervals beginning immediately thereafter (4 men) or after 15 min recovery from the exercise (6 men). No cases of bends pain occurred, but one man exhibited 1° abdominal gas pain at 1 hr, 3° at 2 hrs, 4° at 3 hrs and 5° at 4 hrs. The remaining six men were given only two high-altitude tests--immediately after exercise, and at the end of 2 hrs. Three had no symptoms, one showed a 1° ankle pain at 39,000 ft during the first test and the other two had more severe pains. One of these cases reported an ankle pain of 1° at 26,250 ft and 2° at 31,000 ft on the first test that was absent on the second test. He also had 3° abdominal gas pain at 40,000 ft on the first test and 2° at 40,000 ft on the second test. The other case had 1° knee and ankle pains on the first test, the critical altitude being 33,000 ft. On the second test the ankle pain was absent, but the knee pain responded at the following critical altitudes: 1° at 27,000 ft, 2° at 29,250 ft, 3° at 31,250 ft, 4° at 33,000 ft, and 5° at 35,250 ft.

These results may be summarized as follows: In 32 men showing no symptoms whatever during storage at 15,000 ft, the high altitude tests showed mild bends that receded in two cases (6.3%) and severe bends developing progressively though "silently" during storage in one case (3.1%). Abdominal gas occurred in the same proportion.

SECTION V

IN-FLIGHT DENITROGENATION

Heavy Exercise Series

Twenty of the men in the series described in the preceding section were kept at 38,000 ft from 1½ to 2 hrs after the silent bubble experiment, in order to test the effectiveness of the 15,000 ft storage as an in-flight denitrogenation procedure. In four of the men, (the ones who had somewhat less than 4 hrs of in-flight denitrogenation), three showed 1° pain appearing within 12 - 40 min after reaching 38,000 ft and regressing later. The other case also had bends, beginning with 1° after having been at the high altitude 28 min, and reaching 4° intensity 18 min later. He was then removed from the altitude chamber. These four men did the step-up exercise at 2½ min intervals for the first 45 min at 38,000 ft.

The other 16 men, with a full 4 hrs of in-flight denitrogenation and exercise at 15,000 ft, went to 38,000 ft for 2 hrs with exercise as above. Six were symptom-free, seven had bends that receded (five went to 1° only, one went to 2° and one to 3°). Two men were forced to descend, one with bends that reached 4° after 24 min exposure, and one with chokes at 26 min. One man (not included in the statistics) went only to 35,000 ft because of abdominal gas pain. He developed no bends, but had to descend after only 44 min of exposure.

Eight additional men had no "tests" or exercise during the 4 hrs of in-flight denitrogenation, and exercised only during the second hour at 38,000 ft. Six were symptom-free. Two men developed serious symptoms after the exercise began. One man had bends pain that reached 4°, causing descent at 1 hr 33 min (i.e. 33 min after he started exercise). The other man had 4° bends and a vasomotor reaction (VMR) indicative of impending collapse at 1 hr 54 min.

Summarizing these data, and correlating with the preceding section, the following implications may be derived: Silent bubbles can originate at 15,000 ft when there is exercise. In most cases they are small in magnitude and recede during 3 or 4 hrs. If there is heavy exercise at this altitude, there will be an occasional case (3%) of profuse sub-clinical bends that will cause immediate trouble upon ascent to higher altitude. While the in-flight denitrogenation that occurs while breathing pure oxygen at 15,000 ft exerts a considerable protective influence, it is inadequate for reasonable protection against exposure to 38,000 ft if there is heavy exercise at this higher altitude. In this situation, moderately severe bends or chokes can be expected in 18.5% ± 7.6% cases, since five cases of this type were observed in 27 men. The total incidence of symptoms was 56%. Controls were obtained on 13 of the men, who repeated their

38,000 ft schedule without any type of oxygen pre-breathing. Forty-six per cent descended with chokes, 4° bends or 5° bends; 54% had 3° bends or worse; the total symptom incidence was 85%. These figures cannot be used as a fair quantitative test of the validity of preoxygenation tables previously reported (5, p. 19), which predict a much larger effect from the denitrogenation. No more than moderate physical activity is presumed by those tables. Furthermore, the number of individuals in the sample is rather small. Regardless of qualifications, the observation of serious symptoms in nearly a fifth of 27 men tested is adequate grounds to deny that the denitrogenation afforded satisfactory protection.

Cause of Poor Protection

There are indications within the data of the present study that the inadequacy of the protection is chiefly due to the exercise at the higher altitude, inasmuch as the time of the serious symptoms is apparently related to the time that the heavy exercise occurs. The nitrogen component of the gas bubbles that presumably cause the pain or other symptoms is of course reduced by breathing pure oxygen, either at ground level or in flight at 15,000 ft. On the other hand, this procedure can have no influence on the local concentration of carbon dioxide, which is probably the main causal agent that is responsible for exercise increasing the incidence and severity of aeroembolism (3, pp. 232-233). There has however been some controversy concerning the importance of carbon dioxide--Ferris (3, p. 33) dismisses the systematic experimental evidence (3, p. 232) while Cook, (3, p. 230) questions the interpretation that Ferris has placed on his own data, concluding that it actually supports the carbon dioxide hypothesis. The "exercise limit" emphasized by Jones in his analysis of preoxygenation data (3, pp. 304-306; 8, p. 51) is very likely a reflection of the importance of carbon dioxide. Animal experiments with preoxygenation also demonstrate the role of carbon dioxide in bubble formation (3, p. 150 and 154).

The above line of reasoning would seem to lead to the hypothesis that the relative influence of exercise on aeroembolism should be markedly increased under denitrogenated conditions. While this particular idea has never been tested by systematic experimentation on humans, there is certainly ample evidence that dependable protection for exercised exposure gained by preoxygenation at ground level often requires far more than four hours of denitrogenation. Unfortunately, not all the available data on preoxygenation can be accepted at face value (3, p. 253 ff.).

If, for example, an individual is repeatedly exposed to aeroembolism altitudes in a series of experiments involving progressively longer periods of preoxygenation, until in one of these experiments he fails to have symptoms, it is quite wrong to naively conclude that this amount of denitrogenation has been shown to "protect" that individual. On the contrary, there is a fairly high and known probability that the absence of symptoms is simply a reflection of intra-individual variability (3, pp. 325-330; 8, pp. 147-153). In two flights under the same conditions, results from five different laboratories have shown that on the average about 40% of men forced to descend in one flight remain up in the other, and about 18% of men who remain up in one flight are forced to descend in the other. Figures on symptoms *vs.* no symptoms are similar to the above. (Assuming constant reproducibility, such percentage figures will vary depending on the incidence in the particular group) (3, p. 336 ff.; 8, p. 161).

For this reason, definition of the amount of preoxygenation required for the protection of a particular individual requires that he be repeatedly tested at that particular dosage. Similarly, the protection afforded a group of individuals cannot be estimated unless the data of all members of the group are included, quite regardless of whether or not certain of the individuals in the group may have seemed to be "protected" by a lesser amount of preoxygenation. Interpretation of published data on the amount of preoxygenation required for protection must be conditioned by these harsh but realistic facts; dependable protection is more difficult to achieve than is commonly realized.

Light Exercise Series

It has been emphasized in another report that insofar as predictions can be made from available data, four to six hours of denitrogenation will afford adequate protection "provided that muscular activity be limited to mild and infrequent exertion" (5, p. 1). This is admittedly a rather un-precise statement. Estimations of the amount of activity ordinarily engaged in by flight personnel in the military situations where aeroembolism is anticipated are also difficult to quantify. Wide differences in opinion have been voiced. Having interviewed a number of B-36 personnel and inspected the various positions in this particular aircraft, the writer is of the opinion that the amount and type of activity under the conditions of interest should be defined as light activity, probably comparable on the average to card-playing with occasional periods of standing up and stretching. The writer is unable to state a dogmatic opinion as to how typical this is of the activity in other aircraft of current interest. If personnel are wearing pressurized T-1 suits, it is fairly certain that heavy exercise will be uncommon. Under emergency conditions, it may sometimes happen that a particular crew member will find it necessary to engage in heavy exercise. If so, his probability of having severe aeroembolism will thereby be greatly increased. However, it is not certain that even 8 or 10 hours of denitrogenation will guarantee protection in this circumstance (although the probability of trouble would be lessened).

In the light of the above considerations, and because of other reasons for interest, data on a standardized series of in-flight denitrogenation tests with light exercise have been secured. The activity was card-playing as described in the previous paragraph. Two flight profiles have been used. In one, the men breathed ambient (cabin) air for 1 hr at 10,000 ft followed by 3 hrs on undiluted oxygen at 15,000 ft and 3 hrs high altitude exposure at 38,000 ft. Reasoning from the data shown in Figs. 5 and 6, it seemed likely that there should be very little difference between the effectiveness of this profile and a "standard" profile using full oxygen at 15,000 ft during the first hour as well as the subsequent 3 hrs before the high altitude exposure. Should the experimental facts support this hypothesis, it would be possible to come closer to achieving the recommended amount of denitrogenation (5, p. 2) in operational flights, while at the same time conserving oxygen and lessening the amount of discomfort to personnel that is unavoidable with the recommended special oxygen discipline.

It was also thought desirable to secure a control series, using the same conditions of exposure at 38,000 ft, but reducing denitrogenation to a minimum by starting the oxygen supply at 12,000 ft on the way up, with a fast ascent. It was realized that the control series would not represent ideal data, since we were not permitted intentionally to carry the men to the point of true in-

capacitation. Nevertheless, it would serve to give some indication as to what would happen without the denitrogenation, and could tie in the present data with experimental work done in this laboratory some years ago as well as data from other sources.

A total of 29 men were tested on the 10,000-15,000-38,000 ft profile and 29 on the 15,000-15,000-38,000 ft profile, with 52% of overlapping individuals in the two groups. In other words, in the two combined there were 58 tests on 43 individuals. The control series consisted of 40 individuals, overlapping 90% with the first-named denitrogenation group and 80% with the second or standard group. Of the controls, 62% of individuals did the control after having done a denitrogenation test. Nearly every person used in any of these series had previously seen bends in one of the other experiments described earlier and a majority of them had previously experienced and reported the pain themselves at one time or another. The individuals are thought to constitute an unselected sample.

Experimental Results

The results are shown in Table 4. There was no case of true incapacitation in either of the in-flight denitrogenation groups, although there is a possibility that the individual who was ordered down after 1 hr 28 min because his pain reached 5° in the 10,000-15,000-38,000 ft test might have become incapacitated if he had remained at 38,000 ft. There is also a good possibility that he might not have become incapacitated. It really makes very little difference just how this individual is classified. It is difficult to define incapacitation in the absence of syncope or paralysis; moreover an occasional case of serious bends is sure to occur with even considerably more denitrogenation than used in these tests (3, p. 253).

It should also be mentioned that one individual in this group (who had a 2° bends pain at 1 hr 33 min which thereafter regressed) became nauseated just eight minutes before the end of the 38,000 ft exposure and was taken out at once for reasons of safety. His blood pressure was normal and he had no symptoms of the type usually associated with impending vasomotor collapse, except sweating. It was his own opinion, with concurrence by the physician, that the nausea was due to the fact that he had been up most of the previous night, and, contrary to instruction, had eaten no breakfast before the beginning of the 7 hr altitude chamber flight. His nausea persisted for about 1 hr after descent before any substantial improvement occurred. Otherwise, recovery was uneventful. Uncomplicated, late appearing nausea is not a common symptom of aeroembolism; this man's symptoms may or may not have been related to the high altitude exposure.

All subjects in the 15,000-15,000-38,000 ft group completed the full 3 hrs at 38,000 ft. One case had a bends pain that developed to 4° after 51 min at high altitude; this pain regressed to 3° but did not disappear. This individual had discomfort, but showed no evidence of incapacitation. On the whole, the symptoms tended to be slightly less severe in this group, but this is simply a random variation or "sampling error" because the control tests of individuals in the group also show somewhat fewer and less severe symptoms than men in the other group; descents due to 4° or 5° bends, or to chokes or VMR, was 44% com-

pared with 59%. While this difference is not statistically significant ($\chi^2 = 0.69$), the fact remains that the individuals were on the average less susceptible to severe aeroembolism than in the other group; the effectiveness of the denitrogenation was no greater.

Effectiveness of First Hour on Air

Compared on the basis of the incidence of 2° pain or worse, the two sets of controls are perfectly matched at 52%, and the two denitrogenated groups are also perfectly matched at 17%. Compared on the basis of total symptoms, the "air" denitrogenation group had fewer symptoms; on the basis of 3° or worse it had more symptoms. In neither case is the difference statistically significant, even though it be assumed that the intercorrelation was as high as r = 0.60, which is a too-generous allowance (3, p. 341). Compared on the basis of 4° symptoms or worse, there is no difference. It is therefore necessary to conclude that the first hour of a 4 hr in-flight denitrogenation procedure is practically as effective utilizing ambient air breathing at 10,000 ft as using pure oxygen at 15,000 ft, even though the alveolar nitrogen differential is somewhat less (during that hour). There is every reason to believe that this finding would hold true if the oxygen breathing were extended to a longer period; it may or may not be true for shorter periods.

It cannot be claimed that these results have definitely proved that there is no difference whatever in the effectiveness of the two profiles. All that can be concluded is that any such difference must be very small and unimportant practically, as otherwise it would have become manifest in the comparison of the two well-matched groups.

There is now justification for combining the two series in order to secure a more reliable prediction of the results to be expected with 4 hrs of in-flight denitrogenation. To do this, it is desirable to first average for each individual the results of his two tests (if he had two); some individuals were tested in both series and some in only one. The size of the sample is 43 men.

Table 4

PROTECTION FROM DECOMPRESSION SICKNESS

Secured from two profiles of in-flight denitrogenation, compared with non-denitrogenated exposure to high altitude

Type of symptoms observed at 38,000 ft	1 hr 10,000 air 3 hrs 15,000 O_2 3 hrs 38,000		4 hrs 15,000 on oxygen and 3 hrs 38,000		Control, no denitrogenation 3 hrs 38,000	
	n	Cumulated per cent	n	Cumulated per cent	n	Cumulated per cent
Completely symptom-free	22	76%	19	66%	11	27½%
Minor transient 1° pain	2	83%	5	83%	2	32½%
Mild 2° pain, regressive	3	93%	4	97%	2	37½%
Moderate 3° pain, regressive	1	97%	0	97%	2	42½%
Non-regressive 3° pain	0	97%	0	97%	1	45%
Moderately severe 4° pain*	1	100%	1	100%	13	77½%
Bends with VMR	0	--	0	--	2	82½%
Mild or moderate chokes	0	--	0	--	1	85%
Chokes with VMR	0	--	0	--	3	92½%
Chokes with bends and VMR	0	--	0	--	2	97½%
VMR and dizziness without other symptoms	0	--	0	--	1	100%

*Due to the enforcement of a conservative exposure policy on this project, cases of 4° pain were automatically removed from the chamber. One-third of the control cases having 4° had progressed to 5° during the removal process. In the denitrogenated tests, the individual with moderately severe pain in the "air plus oxygen" series was ordered down in accord with this practice, with momentary 5° pain. He was not incapacitated, looked well, and probably could have "sat out" his bends since they exhibited a relatively flat-topped growth curve of the type that frequently regresses. The corresponding individual in the series involving 4 hrs at 15,000 ft was permitted to remain in the chamber, with some tendency toward regression during the last hour at 38,000 ft.

Probability of Symptoms after Four Hours Denitrogenation

The prediction from the data is: Symptom free or minor 1° pain, 83.7%±5.7%, symptom free or no more than moderate 3° pain, 94.2±3.6%; moderately severe pain that may or may not regress within 3 hours, 3.5%±2.8%; incapacitation, no definite figure possible but not to excede an occasional case per 50 to 100 exposures (i.e. 1 or 2%).

These figures (divided by 100) represent the average individual probability of casualty. To apply them to a practical situation, it is necessary to consider the size of the air crew and the number of essential positions in the aircraft. Methods for doing this are available (5, pp. 11-12). For example, using the 1% casualty figure and considering all crew members essential, a three-place aircraft would have a probability of $0.99^3 = 0.97$ of completing the mission and the abortion rate would be 100 - 97 = 3%. For a ten-place aircraft, the computations would be $0.99^{10} = 0.90$ probability of completion and 10% abortion. Assuming an individual casualty rate of ½%, the abortion rate would be 1% for a 3 man crew and 2½% for a 10 man crew; assuming a 2% individual figure, the abortion rate would be 6% for a 3 man crew and 18% for a 10 man crew.

The data were secured at 38,000 ft, as our safety restrictions did not permit prolonged exposure to any higher altitude. Figure 2 (Section I) offers a basis for estimating that at 40,000 ft the pains would have been about 1° greater, so the expectation would be 5.8% ± 4% of moderately severe or severe pain at that altitude with a somewhat increased probability of incapacitation.

The over-all picture of symptoms after denitrogenation displayed in Table 4, together with the details of the original protocols, leads to a not-entirely-imaginative visualization as follows: A considerable number of individuals in the series have no aeroembolism whatever. These men would have no symptoms on this particular exposure even though the altitude was increased considerably. Another and sizable group has aeroembolism in some degree; in most of these cases it is at a sub-clinical level and would be revealed if the altitude were to be increased sufficiently. The next most frequent type of case actually has clinical bends, usually late appearing and transient at the exposure altitude used, but potentially more severe should the altitude be increased. A few individuals actually have moderately severe aeroembolism, which would be severe at a higher altitude. With more denitrogenation before the high altitude exposure, this "curve" would be shifted to the left; the number of clinically important cases as well as the sub-clinical cases would decrease. With less denitrogenation the curve would shift to the right; the limiting situation would then be the un-denitrogenated exposure, with a majority of the cases clinically severe; perhaps 5 or 10% would be free of aeroembolism and about 20% would have clinically silent aeroembolism that would appear at a higher altitude. This picture is dynamic; it is not at all a matter of individuals being either definitely protected or unprotected by some magic critical dosage of preoxygenation; there is an interplay of a number of physiologic and environmental factors whose influences are in general known and understood, but predictible only in terms of statistical averages.

It may be mentioned at this point that the heavy exercise denitrogenation series showed a much higher incidence of severe or moderately severe symptoms, 18.5% compared with 3.5% in the light exercise series. Using a one-tailed "t" distribution, which is the appropriate statistical hypothesis in this particular

case, the difference is definitely significant ("t" = 1.67 required, 1.85 observed). The fact that the observed symptoms of this type were not only more numerous but also more severe adds further weight to the conclusion.

Control Group

The number and severity of symptoms in the control group may seem surprisingly high. It is not; the total incidence is in fact in excellent agreement with the first extensive standardized series of 38,000 ft exposures at this laboratory during the 1942-45 researches (6, p. 48, designated Series A*). That is the series in which the physical activity was very similar to that of the present experiment. A total symptom incidence of 75.5% was observed, which may be compared with the present incidence of 72.5%. The difference is non-significant since "t" = 0.15. Compared at the level of 3° symptoms or worse, the figures are 55.3% and 62.5%; "t" = 0.70 which is again non-significant. Direct comparison of incapacitation rates is not possible. It may be noted that the earlier series resulted in 42.1% incapacitation while the current experiment resulted in 55.0% individuals with 4° pain or worse symptoms. If we make the reasonable assumption that only half of the cases of 4° pain would have become incapacitated, the agreement would be almost exact. It would accordingly seem that the subjects and techniques of the current experiment have yielded representative results.

Validity of Preoxygenation Tables

In using the data of the present experiments to validate the Jones preoxygenation tables (3, p. 318; 8, p. 98), his factor of 90.7% protection or 9.3% remaining aeroembolism is employed as the probable protection coefficient for 4 hrs of preoxygenation. (In the table as printed, the figures have been rounded off to 91 and 9%). Multiplying the symptom rates in the control by 9.3 we have the expectation of 5.1% of 4° or worse symptoms, compared with the actual observation of $3.5 \pm 2.8\%$; 5.8% of 3° or worse symptoms compared with the observation of $5.8 \pm 3.6\%$. The agreement is very close indeed; the Jones tables are valid for symptoms of this type.

The discrepancy is considerable for symptoms of 2° intensity or worse (6.3% predicted vs $16.3\% \pm 5.7\%$ observed), although it is possibly within the limits of sampling error. However, when the minor 1° pains are included in the total symptom incidence, the prediction from the tables, 6.7%, is not very close to the observed incidence of 29% after in-flight denitrogenation. There is a temptation to dismiss these 1° minor pains, which were reported by 13% of subjects who were otherwise symptom-free, as being non-existent in most cases. It is quite true that with an introspective set for pain observance, it might be expected that after having been in the altitude chamber for approximately six hours, some of the men would occasionally report minor joint pains that are in fact not bends. On the other hand, it has been a consistent observation in other preoxygenation experiments of shorter duration that the per cent reduction in moderate or severe symptoms is greater than for mild symptoms. In the Fraser stepwise ascent data (2) for example, 1 hr on oxygen at 10,000 ft only reduced the mild symptoms 15%, although moderate and severe symptoms were reduced 63%; in his 20,000 ft experiment the mild symptoms increased although moderate and severe symptoms were greatly reduced. In the three preoxygenation experiments reported by Henry and Cook (7), the reduction in symptoms of 3° or worse was always greater than the

reduction in total symptoms; indeed, one of the conclusions of that study was that the principle effect of the denitrogenation is to reduce the intensity of symptoms, rather than to delay their onset by an amount that is of practical importance.

It is entirely reasonable for preoxygenation to result in a greater proportion of minor symptoms than is observed in the controls-in fact, that is exactly what would be expected in the situation where there has been enough denitrogenation to almost but not quite prevent the occurrence of perceptible pain. The use of available denitrogenation tables must therefore be conditioned by the realization that they are valid for predicting the reduction in the serious types of aeroembolism, but over-estimate considerably the reduction in total symptom incidence. This error may be expected to be cumulative; it probably increases with longer periods of denitrogenation. It may be noted that the use of such tables is ordinarily concerned with severe symptoms.

Jones has also prepared tables for the in-flight denitrogenation situation with air breathing at 10,000 ft followed by denitrogenation with pure oxygen (3, p. 320; 8, p. 100). It must be kept in mind that he had very little basic experimental data available for these particular tables, and for some reason did not take into account the increase in denitrogenation rate caused by mild hypoxia as mentioned earlier in Section III. It would accordingly be expected that these tables would under-estimate the protection. The data of the present experiment support this argument. For the air-oxygen profile the observed figures are 3.5% symptoms of 4° or worse compared with 7.7% predicted from his tables and 6.9% symptoms of 3° or worse compared with 8.8% predicted. In the case of minor symptoms the tables are not applicable; this matter has been discussed in preceding paragraphs.

In-flight denitrogenation tables recently prepared by the writer (5, p. 19) do not require the "hypoxia" correction since there is presupposed at least 4 hrs of ambient air breathing at 10,000 ft which would very nearly reach the maximum possible denitrogenation for this condition even with the slower rate used by Jones. The use of this table may however be extended since the faster rate would achieve 90% of the maximum in $1\frac{1}{2}$ hrs and almost completely reach it in 2 hrs. It should be emphasized that this amount of denitrogenation (which is a valuable supplement to the greater amount secured later by breathing pure oxygen) will be lessened if the cabin altitude is lower than 10,000 ft. The experimentally determined incidence of serious symptoms after either of the flight profiles of the present study indicates that the protection is somewhat greater than predicted by the writer's tables. It is recommended however that the tables be used as a basis for planning, since it cannot be expected that the oxygen discipline will be as carefully followed under operational conditions as has been the case in the laboratory situation. As it stands the table is probably applicable without qualification to 40,000 ft exposures.

DENITROGENATION AND SYMPTOM DELAY

Amount of Delay

It should be re-emphasized that denitrogenation, whether accomplished in flight or at ground level, has only a small influence on the time of symptom appearance (7, p. 355). The onset time of symptoms is correlated with their eventual severity; on the average, late-appearing symptoms tend to regress and are usually less severe than the early-appearing type (3, p. 334; 8, p. 158). With denitrogenation, these early and severe symptoms are converted to the later and milder type, while the formerly mild and late have been so weakened that they are sub-clinical. (The terms "early" and "late" are of course entirely relative, since symptom onset times occur in a continuous distribution). Data from the present experiments are in agreement with these concepts.

Table 5

ORIGINAL ONSET TIME OF SYMPTOMS

Arranged according to the eventual severity attained during the 7 hr flights. The beginning of just noticeable pain is stated in minutes after reaching 38,000 ft. (Entries in parenthesis give the time of maximum severity for the case listed directly above).

Maximum Pain Intensity				
1°	2°	3°	4°	5°
60	44	60	47	50
73	58	(70)	(52)	(88)
100	60	--	--	--
103	80	--	--	--
104	90	--	--	--
116	101	--	--	--
120	110	--	--	--

In Table 5, it may be seen that after 4 hrs of in-flight denitrogenation, the symptoms of possible practical importance have had an onset within the first hour after reaching 38,000 ft and have reached their maximum intensity within a half hour thereafter. Bends pain that never went higher than 2° began on the average about 20 minutes later than the initial onset of the more severe pains. The average onset time of the minor 1° pains was about 20 minutes later than for the 2° pains. In these 58 tests, there was no instance of a new case of bends appearing after 2 hrs at 38,000 ft. This means, of course, that the incidence of aeroembolism does not accumulate hour by hour as the exposure time is lengthened. On the contrary, the first 2 hrs at high altitude represent the hazardous period. Occasionally, a severe case may occur later than this, but the evidence indicates that such a circumstance will be rare.

It should be pointed out that the data of Table 5 are completely at variance with certain theoretical contentions that have been advanced by others (3, p. 255-257). If it were true that denitrogenation functions by delaying symptom appearance, the observed data could only be accounted for by postulating that the reactors in the present group had unusually slow nitrogen elimination rates since their delay was less than an hour, the non-reactors had very fast rates since their delay was more than three hours, and there were no average men with middle-of-the-road rates of nitrogen elimination. This is entirely unreasonable. The present writer is accordingly forced to reject the theory in favor of the Jones theoretical explanations (3, p. 298 ff.; 8, p. 40 ff.) which do agree with the observed facts of the current experiments as well as other published data.

In the control series, the average onset time of all symptoms was 49 min. In the denitrogenation series, the figure was 81 min. This onset delay of 32 min may be compared with the Henry and Cook (7) report of 22 min delay in an older group that was less well protected by 4 hrs of preoxygenation. In neither case is the delay of impressive magnitude. Another way to calculate the delay is to compare the onset times of the control and denitrogenated groups at equal percentiles, which would in effect equate the individual nitrogen elimination rates. (Since the intercorrelation of rates on two different days is by no means perfect, this method will bias the average in favor of a longer delay). This has been done with the data as arranged in Fig. 9. Computed in this manner, the average delay is 70 min when there is 4 hrs denitrogenation. The prophylactic value of denitrogenation must therefore be explained in terms of reduced symptom intensity rather than in delay of symptom occurrence.

Theoretical Time of Onset

A previous report (5, p. 5) gave several illustrations of the use of the formula

$$dy/dt = a_1 e^{-k_1 t} - a_2 e^{-k_2 t}$$

to describe mathematically the rate of appearance of aeroembolism symptoms in a group of individuals exposed to high altitude. Nims has used this type of formula to give a theoretical explanation of the physiology of bubble growth and decay, identifying k_1 with the diffusion constant governing the exchange of nitrogen between the tissues and alveolar air, and k_2 with the diffusion constant for the gas exchange between the tissues and the pain-causing bubble (3, p. 213). Simplifying his formula 41 by dropping the constant term, which may be done by using the delayed onset time, 32 min, as t_o (the point at which symptoms will first exceed threshold magnitude and a_1 will equal a_2), it is possible to describe mathematically the rate of new cases of aeroembolism per 100 men per 5 min elapsed time. The appropriate numerical values are $a_1 = a_2 = 3.53$; $k_1 = 0.0133$ and $k_2 = 0.077$. The "half-time" rate coefficients (defined as $0.693/k$) for these k's are 9 min for the symptom growth rate and 52 min for the denitrogenation rate that controls the decline of symptom incidence. The latter figure is reasonably typical for this stage of denitrogenation (5, p. 16).

A curve of this function is shown in Fig. 8. The integral of the curve is drawn as a smooth line in Fig. 9, where it is compared with the experimentally obtained points giving the onset of symptoms during the denitrogenated high altitude exposure. While no new cases actually appeared during the last hour

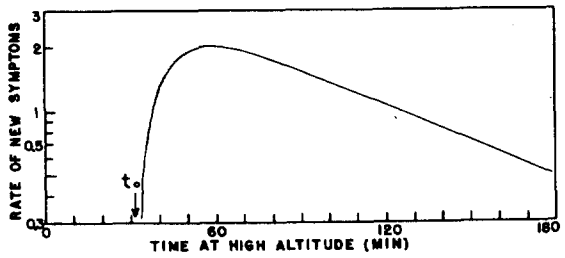

Figure 8. Rate of appearance of aeroembolism cases. (per 100 men per 5 min.) after 4 hrs. of denitrogenation

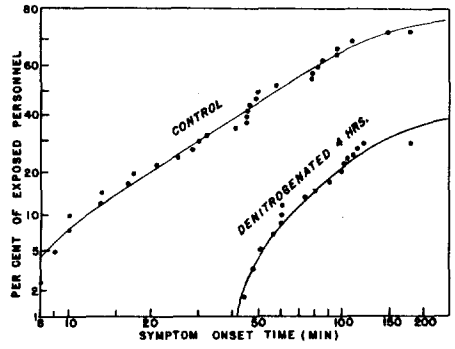

Figure 9. Cumulated incidence of aeroembolism.

of the 3 hr exposure, the theoretical curve predicts that a few new cases should have appeared; there should have been 8.8 per 100 men, (i.e., 5 such cases in the present experiment). No more than 2/17 (i.e. 12%) of these 5 cases would have been expected to have symptoms as severe as 4° pain. In view of the tendency of the late appearing cases to be less severe, there is reason to believe that this proportion ought to be even smaller. With a fourth hour of exposure, the curve predicts 4 new cases per 100; probably none of these would be severe. It should be mentioned that it was not possible to draw a theoretical curve for severe symptoms because the incidence of such cases was too small to furnish the necessary basic data.

As a matter of minor interest, the cumulative incidence of new cases in the control series has also been plotted in Fig. 9. The two curves, control and denitrogenated, both approach an asymptote. They appear superficially to be of different form, but this is simply a by-product of having plotted the data on the usual probability ordinate, using however a logarithmic abscissa in order to obtain even spacing of the points. (This statement can easily be verified by plotting the curves on linear coordinates). The formula is the same for both curves, except that for the controls, t_o is taken at 3 min. The curve constants are of course different; for the controls, the intercept at t_o is higher ($a_1 = a_2 = 8.25$), the growth component is much faster ($k_2 = 0.266$), and the denitrogenation rate is somewhat faster ($k_1 = 0.0198$) since the high altitude exposure has occurred at an earlier position on the complete denitrogenation curve (5, p. 16).

While the denitrogenation rate of 52 min half-time calculated from Fig. 9 and shown as the descending limb of Fig. 8 is of representative magnitude, it is 30 or 40% faster than would be observed at 30,000 ft or lower altitude (3, p. 309; 8, p. 55). For the purpose of constructing protection tables, a representative rate for young men is 70 min half-time. The Jones tables used this figure for "probable protection". As the present experiment has confirmed the predictions from his table, no modification appears to be indicated. Some further explanation of the practical use of his method will be given in the next section.

SECTION VI

RENITROGENATION SUBSEQUENT TO IN-FLIGHT DENITROGENATION

Loss of Protection

Interest in this topic stems from the practical question of how soon susceptibility returns when an individual with regressed aeroembolism (either manifest or silent) at high altitude, resumes ambient air breathing at low altitude or at ground. Apparently this has never been investigated experimentally. An equally important practical problem, related but not necessarily identical, concerns the estimation of protection loss when preoxygenation is interrupted by air breathing. Some experimental work on this problem has been reported (3, pp. 264 and 266), although most data have been secured after 8 or 9 hrs of denitrogenation followed by a 5 hr interruption, which unfortunately is not very helpful in a systematic examination of a wide range of conditions.

Two theoretical treatments of the latter problem are available, by Bateman (3, p. 262 ff.) and by Jones (3, p. 313; 8, p. 91). The Jones graphic method is emphasized here because it can easily be used for practical calculations. While it over-simplifies the theory of inert gas exchange by using only a single exponential term instead of the four known to be involved (3, p. 293; 8, p. 83), it is only possible to quantify and validate a single component from clinical aeroembolism data (3, p. 301; 8, p. 43). For this reason, both denitrogenation tables and renitrogenation tables are based on a one-term exponential system. The rate coefficient is most conveniently measured as half-time (defined as 0.693/k, and easily determined graphically).

A typical example might be an individual with a denitrogenation half-time of 70 min (Jones curve J). Having denitrogenated 4 hrs, an interruption of 1 hr would place this individual back to the equivalent of 70 min of denitrogenation, i.e., the last 3 hrs (nearly) of denitrogenation would be lost by the interruption. A 30 min interruption would lose about 2 hrs of denitrogenation; 15 min would lose about 1½ hrs and a 5 min interruption would negate the last 37 min of denitrogenation. An individual who received protection faster than the average would also lose his protection faster if renitrogenation occurred.

Method of Calculation

The writer has on several occasions been requested to explain (at the practical level) the method of making such calculations. Figure 10 is a semi-log plot of per cent symptoms vs denitrogenation time. The straight-line curve, drawn with a 70 min half-time for the rate coefficient, permits the reading of per cent of original symptoms retained after any particular amount of denitrogenation time. Subtracting this figure from 100 gives the per cent protection that appears in the Jones table, e.g. 91% after 4 hrs. Under the assumption that renitrogenation is the mirror image of denitrogenation, a second line is drawn parallel to the first, with the intercept at 91%. Reading on this line, ½ hr interruption by breathing ambient air gives 67% protection retained; 100 - 67 = 33% of original symptoms now present. Locating on the original line the time required for 33% of symptoms retained, it is seen that 1 hr 51 min denitrogenation reduces symptoms to this amount. Subtracting that time from the original 4 hrs shows that the last 2 hrs 9 min of denitrogenation has been lost by the ½ hr interruption. Had the same interruption occurred at 3 hrs instead of 4, the intercept of the auxilliary line would be at 100.0 - 16.6 = 83.4%

protection, there would be 62% of protection retained (38% of original symptoms now present), and the time loss would be 3 hrs minus 1 hr 37 min (i.e. the last 1 hr 23 min of denitrogenation would be negated by the interruption and this additional time would be necessary to recapture the protection that had been achieved by the original 3 hrs).

While the same general principles might be expected to apply to the in-flight denitrogenation-renitrogenation problem, it is necessary to use rate coefficients known to be applicable to the situations under consideration. This modification will be discussed after presenting some illustrative experimental results.

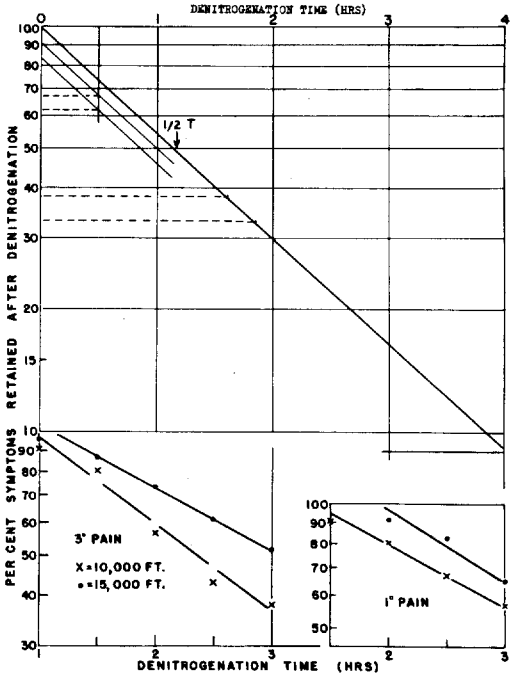

Figure 10. Denitrogenation - Renitrogenation calculations. Insert graphs show data from storage experiments.

Experimental Results

Eight men who were in the 10,000 ft "storage" experiment were persuaded to remain available for a 38,000 ft exposure after renitrogenating by breathing ambient air at ground level. There was pre-established bends of 4° intensity at the beginning of the 10,000 ft storage period. Pure oxygen was breathed during storage. Each man had remained in storage until his symptoms (silent at 10,000 ft but manifest during the "tests" at higher altitude) regressed to the point that they did not show at 40,000 ft. Presumably this regression was caused by in-flight denitrogenation. In the final 38,000 ft exposure after renitrogenation the standard step-up exercise was performed at 2½ min intervals.

Two cases, Nos. 189 and 191, were permitted to renitrogenate for 25 min and then taken to 38,000 ft. While no bends occurred, these two runs are not usable

because abdominal gas pain forced descent after a few minutes exposure. The other 6 cases (with longer renitrogenation periods) are usable. Table 6 summarizes the details. Length of the renitrogenation period is assumed to be the elapsed time from oxygen off during descent from storage to oxygen on at 12,000 ft during ascent for the final 38,000 ft exposure.

To estimate the in-flight denitrogenation rate coefficient, the data from Table 3 (Section III) have been used to plot the points of the insert graphs of Fig. 10. This procedure assumes that the per cent of individuals reacting with bends pain after varying lengths of storage is a measure of the bends-producing nitrogen gas remaining in the group of stored individuals; the rate of reduction in the proportion reacting is therefore a measure of the average rate of in-flight denitrogenation. The 10,000 and 15,000 ft series have both been plotted, since other analyses indicate the results are similar in both. The average half-time denitrogenation rate coefficient from these data, estimated from the straight lines of the Fig. 10 insert graphs, is 100 min. While slightly slower than average rate constants obtained by others with different methods, using ground-level denitrogenation (3, p. 313; 8, p. 91), it is remarkably similar to those determinations. Since the storage series necessarily involved some selection, as it consists entirely of individuals who developed bends in their first 38,000 ft exposure, it would be expected to yield a somewhat slower denitrogenation rate than an unselected group.

Using the method previously explained, with the substitution of the individual denitrogenation and renitrogenation times of Table 6 and the 100 min half-time coefficient, we would expect 61% recurrence for the first two men, 48% for the middle two, and 91 and 88% for the last two men who had over 4 hrs renitrogenation. Assuming a 70 min half-time, these figures would be 60% for the first two, 52% for the second two, and 96 and 94% for the last two men. These calculations assume 100% susceptibility, since each man originally had 4° bends. This may be slightly high, but on the other hand even an unselected group would have a very high symptom incidence with the altitude and exercise used, so the discrepancy cannot be large. Inspection of the 38,000 ft results of Table 6, in relation to the above computations, shows that they are in line with theoretical expectations.

Table 6

DENITROGENATION-RENITROGENATION PROTOCOLS

Bends of 4° intensity had been pre-established at 38,000 ft just before the in-flight denitrogenation started at 10,000 ft breathing pure oxygen.

Subject Number	Length of in-flight denitrogenation	Ambient air at ground	Symptoms at 38,000 ft after renitrogenation
197	2 hrs 4 min	56 min	No symptoms; 40 min exposure.
206	2 hrs 5 min	58 min	1° knee at 9 min, 3° at 12 min; 5° at 15 min; descent.
240	3 hrs 39 min	56 min	Intermittant 1° ankle after 34 min. Exposure 70 min.
223	3 hrs 33 min	57 min	1° ankle after 30 min; fluctuated 0°- 2° for 21 min, and then regressed. Exposure 70 min.
200	3 hrs 21 min	4 hrs 55 min	1° shoulder 31 min; reached 4° at 33 min; descent. (explosive type symptoms)
202	3 hrs 35 min	4 hrs 30 min	1° knee after 16 min; 3° at 19 min; descent at 24 min.

SUMMARY

When aviator's "bends" pain was pre-established by exposure to a decompression chamber pressure equivalent to 38,000 ft, the average critical altitude for disappearance or reappearance of mild pain was 23,900 ft. For moderate pain, the critical altitude was 28,500 ft; for severe pain, it was 31,600 ft. The standard deviation averaged about 20% of the mean. Tables were prepared to show the range of individual differences in critical altitude for the various intensities of pain.

Rapidly repeated ascent and descent of several thousand feet in the region of the critical altitude for bends did not cause any appreciable alteration in aeroembolism symptoms as compared with steady altitude conditions. It was observed that a symptom growth phase occurred during the first 40 min, followed by a symptom decay phase that was progressive. These phases occurred in both variable altitude and steady altitude conditions.

Men with pre-established bends were "stored" without exercise at altitudes ranging from 10,000 to 25,000 ft. When stored at 10,000 or 15,000 ft, the

critical altitude increased progressively with time, resulting in a gain of 12,000 or 13,000 ft in the course of 3 hrs. The percentage of individuals who were bends-free at the maximum test altitude of 40,000 ft also increased progressively, in agreement with a logarithmic law that is characteristic of the known rate of denitrogenation as estimated by other methods and in other circumstances. On the other hand, men stored at 20,000 or 25,000 ft showed relatively small gain in critical altitude during 3 hrs. Observation of a decline in critical altitude during the first ½ hr of storage suggested that "silent bubble" growth at these altitudes might be the causal agent. These results were considered to offer a basis for concluding that in-flight denitrogenation prophylaxis prior to high altitude exposure could be effectively accomplished at 10,000-15,000 ft but not at 20,000-25,000 ft.

Comparison of results at 10,000 ft breathing ambient (cabin) air vs breathing pure oxygen showed that the amount of denitrogenation, as estimated from the change in critical pain altitude, was the same for both conditions during the first 60 to 90 min of storage. Presumably the increase in denitrogenation rate caused by the mild hypoxia when breathing air was as important a factor as the greater nitrogen differential when breathing pure oxygen. After 1 or 1½ hrs time, there was relatively little change in critical altitude during air-breathing whereas it continued to increase during oxygen breathing. The similarity between the two 10,000 ft series during the first hour was not due to the recompression factor, since the increase in altitude was not different from that observed in the 15,000 ft series. These results were interpreted as suggesting that in-flight denitrogenation prophylaxis of several hours duration should be almost fully effective if ambient air instead of oxygen was breathed at 10,000 ft during the first hour. This procedure would result in considerable economy of oxygen and lessened discomfort to flight personnel. The desirability of increasing the cabin altitude to 12,000 or 14,000 ft during the last half hour of air breathing before shifting to pure oxygen was pointed out.

In order to validate existing tables for estimating the amount of denitrogenation via preoxygenation required to prevent severe bends and other dangerous symptoms of aeroembolism, and to confirm directly the conclusions of the preceding paragraph, two types of low altitude in-flight denitrogenation profiles were compared as to their effectiveness in preventing aeroembolism at high altitude. One hour on ambient (cabin) air at 10,000 ft was as effective as 1 hr on pure oxygen at 15,000 ft, when both were followed by 3 hrs on oxygen at 15,000 ft and 3 hrs of test exposure to 38,000 ft with light physical activity. This amount of denitrogenation resulted in the amount of protection against serious symptoms that was predicted for 4 hrs of oxygen breathing by available preoxygenation tables. Under control conditions (without denitrogenation before exposure to 38,000 ft), the incidence of moderately severe or worse symptoms was 55%; after 4 hrs of in-flight denitrogenation the figure was only 3.5%, and there were no cases of chokes, vasomotor collapse or fulminating severe bends although such symptoms were fairly common in the control series. Mild symptoms showed less than the predicted reduction.

Symptom onset at high altitude was delayed 32 min (or 70 min, depending on the method of calculation) as a result of 4 hrs denitrogenation. The observed facts were inconsistent with the hypothesis that the prophylaxis from denitrogenation could be explained by delayed symptom onset. On the contrary, the chief effect was a decreased symptom intensity. The rate of occurrence of symptoms reached its peak within an hour after reaching high altitude and declined rapidly

thereafter at the rate of 52 min half-time, which is a typical denitrogenation rate for 38,000 ft.

With relatively heavy physical exercise during the denitrogenation period at 15,000 ft, silent bubble formation occurred in several cases. When this type of exercise was engaged in at 38,000 ft, it was found that 4 hrs of denitrogenation failed to offer adequate protection against aeroembolism, since 18.5% of the men had chokes, severe bends or related vasomotor reactions. A consideration of the theoretical factors involved (carbon dioxide production in particular) suggested that adequate protection would be difficult to achieve under conditions of heavy exercise.

The in-flight denitrogenation rate estimated from symptomatic evidence of silent bubble decay was observed to have a half-time coefficient of 100 min (somewhat slower than typical rates observed by others at ground level). Renitrogenation at zero altitude, breathing ambient air, apparently progressed as the mirror image of denitrogenation (both being estimated on the basis of aeroembolism occurrence). Individuals who had denitrogenated to the point of symptom disappearance in flight, recovered approximately 50% of original susceptibility in an hour of air breathing and 90% in about 4½ hrs, as predicted by theory.

Symptom incidence in both the control series and the unselected group used to obtain pre-established bends in the storage experiments, compared with the incidence reported some ten years earlier for similar high altitude exposures, indicated good reproducibility and suggested that the individuals used in the present study constituted a representative group of young men. The necessity for standardization of method with consideration of psychological factors was emphasized. In general, the experimental findings in the study were consistent with aeroembolism and denitrogenation theory developed in previous reports from this laboratory.

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APPENDIX I

SYMPTOMS, OTHER THAN BENDS, RESULTING FROM ALTITUDE CHAMBER DECOMPRESSION

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ABSTRACT

1. The most common symptoms resulting from decompression (except for joint pains) were abdominal gas pains, aerotalgia, chokes, syncopal reactions, and scotomata, in that order of frequency. Only one mottled skin lesion was noted.

2. No really serious reactions were produced, and there were no delayed collapse reactions or paralyses. The absence of dangerous complications in these experiments is thought to be due to a policy of rapid removal of subjects from the chamber at the first sign of the development of any of the more hazardous reactions.

The most common symptoms resulting from decompression (except for joint pains) were abdominal gas pains, aerotalgia, chokes, syncopal reactions, and scotomata, in that order of frequency. Only one mottled skin lesion was noted.

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The symptoms which may appear in an individual exposed to reduced atmospheric pressure have already been mentioned briefly in the introduction of this report. Several excellent reviews of these phenomena have appeared in the literature in the past ten years. (1,2,3). Interest has revived in this field recently, spurred on by the development of aircraft which are able to fly higher and higher with each new model produced. It is therefore thought desirable to add to the report a short discussion of the symptoms, other than "bends", which were observed in the experimental subjects while they were at reduced pressures in the altitude chamber.

All of the subjects were male university students, 88% falling in the age group 21-25 years. Prior to their first experimental flight, they were given a medical survey, with emphasis placed on the condition of their ears, nose and throat, lungs, and heart. Any pathology of these structures was sufficient to exclude an individual from the study. In addition, a history of a recent respiratory or sinus infection, recent allergic rhinitis or asthma, and migraine or a convulsive disorder at any time in the past would also disqualify a potential subject from the group.

Following the physical examination and indoctrination lecture, the men were given a short flight to a simulated altitude of 30,000 ft, to familiarize them with the oxygen equipment and with the techniques useful in equalizing the pressure in the middle ear. The descent from this altitude was made at an average rate of 4,500 ft per min. All subjects who experienced great difficulty in clearing their ears were eliminated from future flights.

It should also be mentioned here that it was agreed, at the onset of the experimental work, to take a conservative attitude towards the development of symptoms other than joint pains or gas pains, and it was decided to limit these two manifestations of the reduced environmental pressure to a severity of 4° or 5° (California Altitude Pain Scale). While subjects were in the chamber under reduced pressure, they were under the continuous scrutiny of one inside observer and two or more observers stationed outside the chamber at the observation ports. All of these observers were aware of the nature, manifestations, and treatment of the various reactions which may occur at altitude. When any of them felt that a subject was beginning to display signs of an untoward reaction, the subject was removed from the chamber without delay. Discussions concerning the exact diagnosis of the symptoms presenting themselves, and evaluation of their actual severity, were held afterwards, with the subject out of the chamber.

It is felt that the complete absence of severe reactions, and the relative paucity of all types of untoward reactions, resulted from the pre-flight screening and orientation and the conservative policy described in the above paragraph.

Chest Symptoms

Of a total of 375 man runs in the chamber, 23 cases of "chokes" (3,4) were seen (Table 7). Fourteen of these cases appeared during the storage runs, two during the cycles experiments, one during the heavy exercise series, and six during the in-flight denitrogenation control flights (Table 7). As has been reported by nearly all the observers in the past, there was a significant association between the chest symptoms and joint pains. Of the 23 cases, 13 were classified as mild or incipient chokes, in accordance with Bridge's classification (3), and 10 were rated as moderate in severity. No severe cases were seen, probably due to the rapid removal from the chamber of any subject who complained of a 2^{o} or greater chest pain, or who was observed to be coughing frequently.

With regard to the time of onset of chest symptoms, there appears to be a definite relationship with physical exertion, as is the case with bends. Of the 16 cases seen during the storage and cycles runs, where the subject exercised at 38,000 feet in order to establish bends pain for study during the experiments, 11 cases of chokes appeared in 30 min time or less. Of the six cases seen during the in-flight denitrogenation controls, where there was no regular exercise and the entire flight was made at 38,000 feet, only two cases developed within 30 min, and the other four developed later.

In only a few of these cases did the symptoms become worse during the descent. Nearly all complained of a raw or tight feeling substernally, and three men volunteered the description that the chest sensation was similar to that experienced after running a hard, long race. Deep inspiration made the pain worse in every case.

There were no auscultatory findings present at any time in these men, and all felt well by the time they were removed from the chamber. The only residual then, in several of the cases, was a mild uncontrollable cough on deep inspiration, and in every instance, this had ceased 30 min after the individual had reached ground pressure. Cyanosis was seen in two cases, and it disappeared before the cough did, in both subjects.

Vasomotor Reactions

These reactions have been described and discussed in great detail elsewhere (1,2,3) and their general character will not be set forth here. As far as the cases seen in this series of experiments are concerned, several were probably due to hyperventilation, secondary to anxiety or to severe joint or gas pains. However, this factor is a difficult one to evaluate, particularly in the experimental situation obtaining. There is no doubt that the psychic effect of severe pain is, in some individuals, sufficient to cause a syncopal reaction without the added etiological factor of a respiratory alkalosis.

Only 19 instances of vasomotor reactions were seen in the entire series of altitude chamber exposures, and no actual case of syncope occurred. This latter fact is again probably explained by the prompt removal from the chamber of subjects evidencing premonitory symptoms. Ten of the reactions were seen during the storage-type flights, eight during the in-flight denitrogenation controls, and one during the heavy-exercise series.

Table 7

SUMMARY OF FINDINGS IN SUBJECTS EXHIBITING CHEST SYMPTOMS

Time of onset[1] (min)	Severity Chest Pain	Cough	Bends			VMR[2]
			Mild	Mod.	Severe	
Storage Series						
5	Mod.	Yes	-	Yes	-	-
10	Mild	-	-	-	-	-
10	Mod.	-	-	Yes	-	-
23	Mild	-	Yes	-	-	-
29	Mild	Yes	-	-	-	-
30	Mod.	-	-	-	-	-
30	Mod.	-	-	-	-	-
30	Mild	-	Yes	-	-	-
30	Mild	Yes	-	Yes	-	-
45	Mod.	Yes	-	-	-	-
65	Mild	Yes	-	Yes	-	-
75	Mild	-	-	-	Yes	-
95	Mild	-	-	Yes	-	-
120	Mild[4]	-	-	-	Yes	-
"Cycles" Series						
7	Mild	Yes	Yes	-	-	-
20	Mild	-	-	-	Yes	-
Heavy Exercise Series						
24[3]	Mod.	-	-	-	-	-
In-Flight Denitrogenation Control Series						
30	Mod.	Yes	-	-	-	-
31	Mod.	Yes	-	-	-	Yes
45	Mild	-	-	-	Yes	-
60	Mod.	Yes	Yes	-	-	-
130	Mild	Yes	-	-	-	-
160	Mod.	Yes	-	Yes	-	Yes

1 After arrival at simulated altitude of 38,000 ft.
2 Vasomotor reaction.
3 Preceded by 4 hours at 15,000 ft on oxygen. Exercises every 2½ min after arriving at 38,000 ft.
4 With visual symptoms.

As one might expect from the above discussion, the incidence of these reactions was highest at the time when the bends pain was the greatest. In the storage group, where bends pains were induced by exercising for the first 30 min at 38,000 ft, eight of the ten vasomotor reactions occurred within the first 30 min. In the in-flight denitrogenation control group, without regular exercise at 38,000 ft, only two of the eight cases developed within 30 min.

Even more than in the case of chokes, pallor was found to be the best early sign of an impending vasomotor reaction (Table 8). It preceded subjective complaints by a variable period of time, ranging from a minute or two to 10-15 min. No cyanosis was observed, and since the altitude was never over 40,000 ft, and the fit and functioning of the oxygen apparatus was obvious at all times during the flights (due to the use of rebreather bags and BLB masks), it is unlikely that hypoxia ever was an etiological factor in the reactions seen here. It is of interest that in the in-flight denitrogenation group, kept at 10,000 ft without supplementary oxygen for the first hour of the flight, cyanosis was seen in several of the individuals, and yet no vasomotor reactions occurred during that portion of the flight.

Table 8

INCIDENCE OF RELATED SYMPTOMATOLOGY IN 19 CASES OF VASOMOTOR REACTIONS

Symptom	Incidence	Per Cent of 19 Cases
Pallor	14	74
Nausea	11	58
Diaphoresis	10	53
Dizziness	9	47
Faintness	9	47
Bends-mild	5	26
Bends-moderate	3	16
Bends-severe	5	26
"Chokes"-mild	3	16
"Chokes"-moderate	1	5
Abdominal Pain	3	16
Visual Disturb.	1	5
Headache	1	5

The typical clinical picture presented was one where the subject evidenced marked pallor, with a drenching cold sweat, and complaints, usually of a marked nausea, dizziness, weakness and faintness. In one case, headache was also present. Simply lowering the head well below the knees, with the subject in the sitting position (making sure, the meanwhile, that the oxygen mask remained in place) was sufficient to alleviate the symptoms in all the cases, save one, before the subject had reached a pressure altitude of 10,000 ft, on his way down and out of the chamber. A slight bradycardia (50-60/min) was usually present when the symptoms were at their peak, and immediately after removal from the chamber, the blood pressure was normal in every case, except the one

mentioned above. In his case, it returned to normal levels, when the subject was in the supine and erect positions, within 40 min.

These particular subjects were held at the chamber site, and observed for two hours following recovery from their reaction, and then allowed to leave. Telephonic inquiries as to their status were made during the next 12 hours. All of the subjects in the entire experimental group were instructed to check with the physician 12 hours after their flight, and sooner if symptoms required it. No delayed collapse reactions were seen.

Abdominal Pains

Other than noting the rather high incidence of discomfort due to gas pains at 38,000 ft, little mention will be made of this symptom. Only a small number of runs were aborted due to this cause. Occasionally, when the subject was having great difficulty in passing gas, it was found helpful to partially compress him, and urge him to massage his abdomen and actively try to pass flatus. On many occasions, this procedure enabled the subject to rid himself of the troublesome intestinal gas, whereas previously, at the higher altitude, he had been unable to do so.

Aerotalgia and Aerotitis

Due, probably, to the screening and indoctrination procedures, relatively few individuals developed otalgia during the actual test flights. Use of a vasoconstrictor inhaler or nasal spray helped most of the individuals who had difficulty in clearing their ears by any of the usual methods (swallowing, yawning, grimacing, Valsalva maneuver). The spray, which was of 0.05% naphazoline hydrochloride (Privine HCl) was much more effective than the inhaler.

In spite of these measures, several subjects developed moderately severe aerotitis, but all of these cases subsided within 48 hours with vasoconstrictor therapy alone, and none became secondarily infected. No ruptures of the tympanic membrane were produced.

One individual had the rather harrowing experience of being "trapped" at a simulated altitude of 23,000 ft with severe bends pains in both knees, and severe pains in both ears. Increasing the pressure, to relieve the joint pains, produced excruciating ear pain, and decreasing the pressure, to relieve the ear pains, caused the bends to get much worse. He was sensitive to pressure changes of as little as 500 ft either way, at that altitude. By means of several applications of the nasal spray, and a rate of descent of 200 feet per minute, he was eventually removed from the chamber without laceration of his ear drums.

Three cases of frontal sinus pain appeared during descents, all alleviated by stopping the descent temporarily and using the nasal spray. One slight nasal hemorrhage was also noted.

Visual Disturbances

The only neurologic abnormality which appeared in this series of low pressure exposures was the presence, in a small number of subjects, of scotomata and the headache which usually followed them (1, 5). In 375 man-runs, six cases developed. Five individuals were suffering from bends at the time their visual symptoms appeared. One of the cases developed five minutes after the individual had been removed from the chamber because of mild chokes. The other five all developed while the subjects were in the chamber, although in only two cases were the men at the highest altitude to which they had been exposed. The other three were at their storage altitudes (20,000 ft in one case, 10,000 ft in the remaining two).

The scotomata were discovered in one individual after he complained that he was unable to read; the other five complained of seeing flashes of light or bright spots before their eyes. The scotomata were variously characterized as being scintillating, glistening, or shimmering (Table 9). All of them were multiple,

Table 9

SUMMARY OF CASES WITH VISUAL DISTURBANCES

Description of Scotomata	Associated Symptoms	Time[1]	Headache
Bilateral, multiple, "shimmering"	Bends	30 min	Bilateral, diffuse, lasted 2 hours.
Bilateral, multiple, revolving, "bright"	Bends & Chokes	7 min	Bilateral, diffuse duration unknown.
Bilateral, multiple, "shimmering." Had left homonymous hemianopsia	Bends	3¼ hrs	"Sharp", in rt. occipital region, started 1½ hrs after scotomata appeared. Lasted 6 hours.
Bilateral, multiple, "flashing"	None	30 min	Bilateral, frontal. Started 30 minutes after reaching ground. Lasted 3 hours.
Bilateral, multiple	Bends	10 min	None.
Bilateral, multiple, "scintillating"	Bends	Desc.[2]	Moderately severe left frontal, after 30 minutes at ground. Accompanied by nausea. Subject had migraine previously. Lasted six hours.

[1]Time, in minutes or hours after reaching ground level, for disappearance of scotomata.

[2]Disappeared during descent.

and homonymous, and they were all said to be moving in various ways. Visual field defects were demonstrable by confrontation tests in five of the six cases. Five of the cases were followed by headache. One subject, who had an almost complete left homonymous hemianopsia, began to complain, 1½ hrs after he was out of the chamber, of a severe right occipital headache. The other headaches were more vague in localization, but usually in the frontal region.

There were no muscular paralyses noted during the duration of the project, nor did any of the aphasias appear.

Skin Lesions

Only one significant skin lesion was noted--a mottled skin lesion (1). Many of the subjects noted chilly sensations and itching of the skin, but no record was kept of these findings since they were, in every case, trivial and not troublesome.

The aforementioned subject had severe bends in his left shoulder during a 3 hr storage run. The next morning, he complained of slight pain and swelling in the region of the left pectoralis major muscle. The pain and swelling increased throughout that day, and were accompanied, later on, by a diffuse erythema and increased warmth of the skin overlying the edematous and tender area. No induration or crepitus was present. Forty-eight hours after the flight, this mottled skin lesion began to regress, and 24 hrs later, had almost completely disappeared.

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